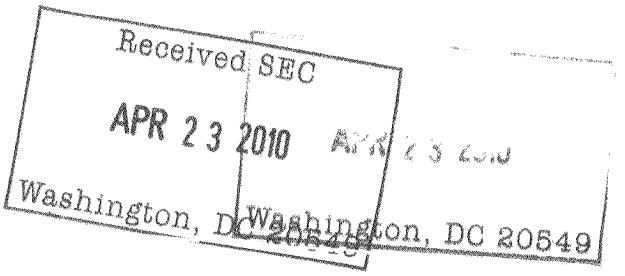


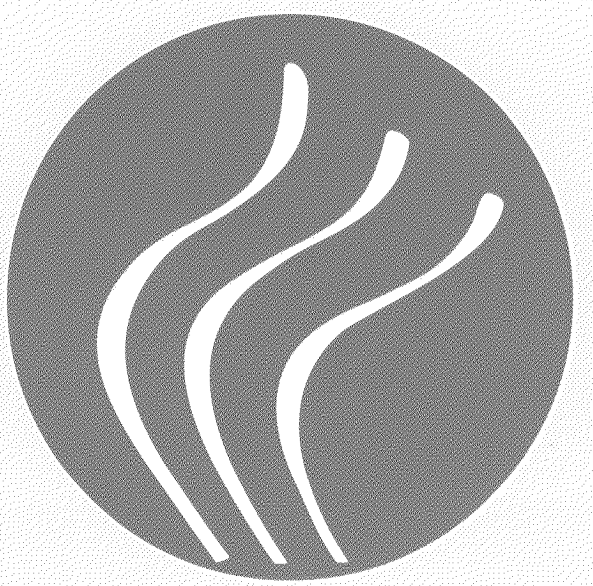
Foundations For Success

INSPIRE

2009 Annual Report

About Inspire

Inspire is a biopharmaceutical company focused on researching, developing and commercializing prescription pharmaceutical products for ophthalmic and pulmonary diseases. Inspire's goal is to build and commercialize a sustainable portfolio of innovative new products based on its technical, scientific and commercial expertise. The most advanced compounds in Inspire's clinical pipeline are denufosol tetrasodium for cystic fibrosis and *Prolacria*™ (diquafosol tetrasodium ophthalmic solution) 2% for dry eye, which are both in Phase 3 development, and *AzaSite*® (azithromycin ophthalmic solution) 1% for blepharitis, which is in Phase 2 development. Inspire receives revenues related to the promotion of *AzaSite* for bacterial conjunctivitis, the co-promotion of *Elestat*® (epinastine HCl ophthalmic solution) 0.05% for allergic conjunctivitis and royalties based on net sales of *Restasis*® (cyclosporine ophthalmic emulsion) 0.05% for dry eye. For more information, visit www.inspirepharm.com.



Adrian Adams
President and Chief Executive Officer

To Our Stockholders,

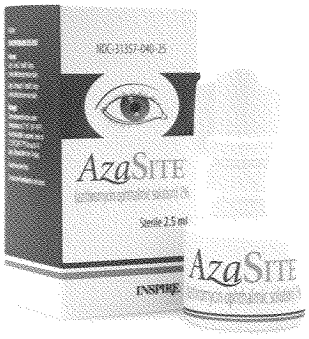
Inspire was founded with a focus towards developing a novel pharmaceutical treatment for cystic fibrosis. Over time, the goal broadened into developing treatments for diseases involving deficiencies in the body's natural mechanisms for protecting mucosal surfaces within the lungs and on the eyes. The Company has made tremendous progress towards that goal as a result of the dedication and hard work of its employees, its Board of Directors and, in particular, my predecessor, Dr. Christy Shaffer, whose vision and determination helped Inspire to create an attractive platform of commercial and pipeline assets—our **foundations for success.**

With that background and legacy, I was pleased to join Inspire in early 2010 to build on this platform and help build sustainable success and shareholder value. I was attracted to the Inspire opportunity for several fundamental reasons. First, I strongly believe in the value of focusing resources on specialty pharmaceutical markets, particularly those with high unmet needs. Inspire's targeted focus on ophthalmology and pulmonology provides excellent anchor programs to leverage in the future. Second, the Company has a stable financial base with a solid cash position, low and declining debt and growing revenues. And finally, Inspire has a powerful corporate culture with an employee base that is experienced, entrepreneurial and highly motivated to achieve long-term success.

2009 ACCOMPLISHMENTS

Inspire had a productive year in 2009 focused on increasing sales of our anchor ophthalmology product, *AzaSite*® (azithromycin ophthalmic solution) 1%, continuing R&D pipeline progress, in particular with our anchor pulmonary product candidate, denufosol tetrasodium, and driving outstanding financial performance, including strengthening our capital position and reducing our debt.

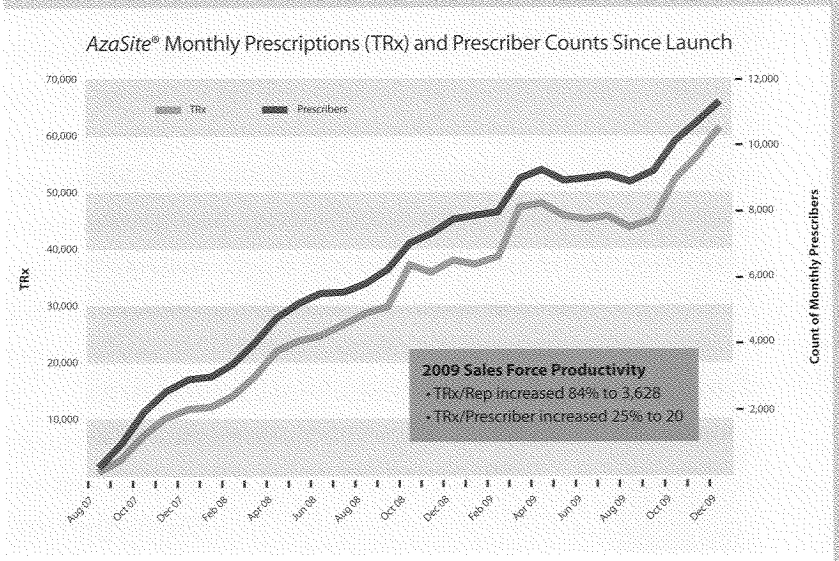
Leveraging Our Commercial Infrastructure and Enhancing Productivity



***AzaSite*® (azithromycin ophthalmic solution) 1%**

- Our team continued to successfully build our ocular anti-infective product, *AzaSite*, increasing prescriptions by an impressive 74% in 2009, which led to a 91% increase in revenue over 2008 to $35 million. Patient and physician usage of *AzaSite* continued to expand, as demonstrated in the chart on this page showing total prescription growth since the launch of the product in 2007.
- We continue to drive enhanced productivity from our sales force with total *AzaSite* prescriptions per representative increasing 84% in 2009 and total prescriptions per prescriber increasing 25%.
- *AzaSite* market share grew in 2009, averaging 11% in our target audience of eye care specialists and 4% among all prescribers, based on the single-agent ocular antibiotic market.
- *AzaSite* revenue was also positively impacted by $3-4 million in 2009 due to a change in the product landscape in which hospitals used *AzaSite* as a substitute therapy during a temporary supply shortage of erythromycin ophthalmic ointment (0.5%).

***AzaSite*®–Enhanced Sales Force Productivity**



***Elestat*® (epinastine HCl ophthalmic solution) 0.05%**

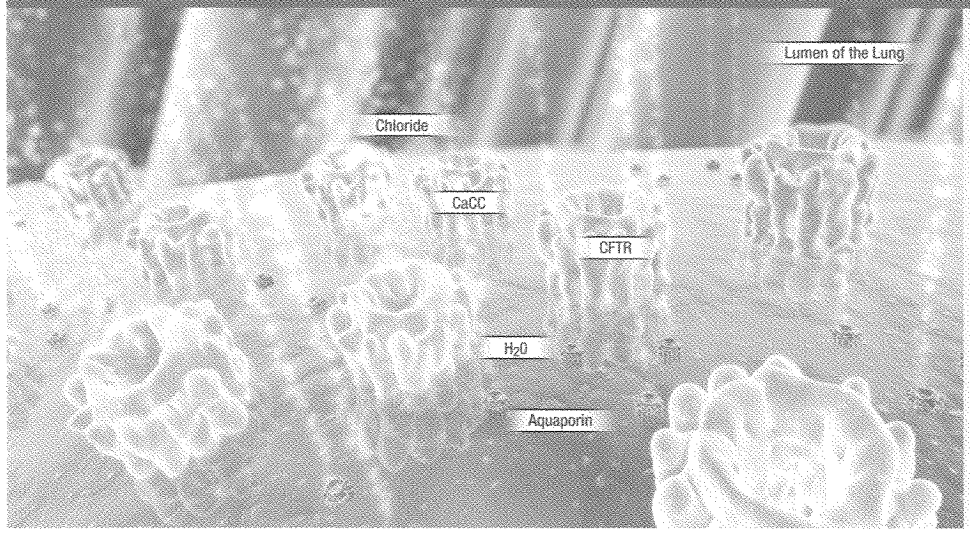
- We maintained a revenue stream of $18 million in 2009 from the allergic conjunctivitis product, *Elestat*, which we co-promote. As we have reported previously, several Abbreviated New Drug Applications (ANDAs) for a generic version of epinastine have been filed and are currently being reviewed by the U.S. Food and Drug Administration (FDA). We anticipate a potential generic product during the second half of 2010. However, until a generic product is launched our sales force will continue co-promoting *Elestat*.

Driving Excellence in Research and Development Execution

Pulmonology Research and Development

- We completed enrollment in TIGER-2, our second Phase 3 pivotal trial of denufosol tetrasodium for cystic fibrosis (CF), in November 2009. We believe the success in enrolling this trial is an indicator of the CF community's strong interest in a new therapy that has the potential to change the course of the disease. Denufosol is a first-in-class ion channel regulator targeted as an early intervention treatment that potentially corrects the ion transport defect in patients with all CF genotypes.
- We presented additional data from TIGER-1, our first Phase 3 pivotal trial of denufosol, at key scientific meetings, including the North American Cystic Fibrosis Conference and the American Thoracic Society and European Cystic Fibrosis Society annual meetings.

A Novel Approach to Treating Cystic Fibrosis



Denufosol is designed to enhance airway hydration and mucociliary clearance by increasing chloride secretion, inhibiting sodium absorption and increasing ciliary beat frequency. These integrated pharmacological actions and the ability to reach the small airways are key to maintaining lung function and potentially delaying the progression of lung disease.

- We continued progress in completing several regulatory requirements needed for a denufosol New Drug Application (NDA) to the FDA. These included reporting safety data from the open-label extension of TIGER-1 and the results from the required two-year inhalation carcinogenicity study.
- We currently are planning for a potential NDA submission in 2011, with a projected launch, subject to FDA approval, in 2012.
- We began significant commercial planning and franchise development activities to enhance our understanding of denufosol and its global opportunity as a potential first-in-class ion channel regulator. We are conducting market research, confirming manufacturing plans, exploring second generation delivery devices and working on strategies to expand our clinical and scientific database on denufosol beyond the two Phase 3 pivotal trials.

Ophthalmology Research and Development

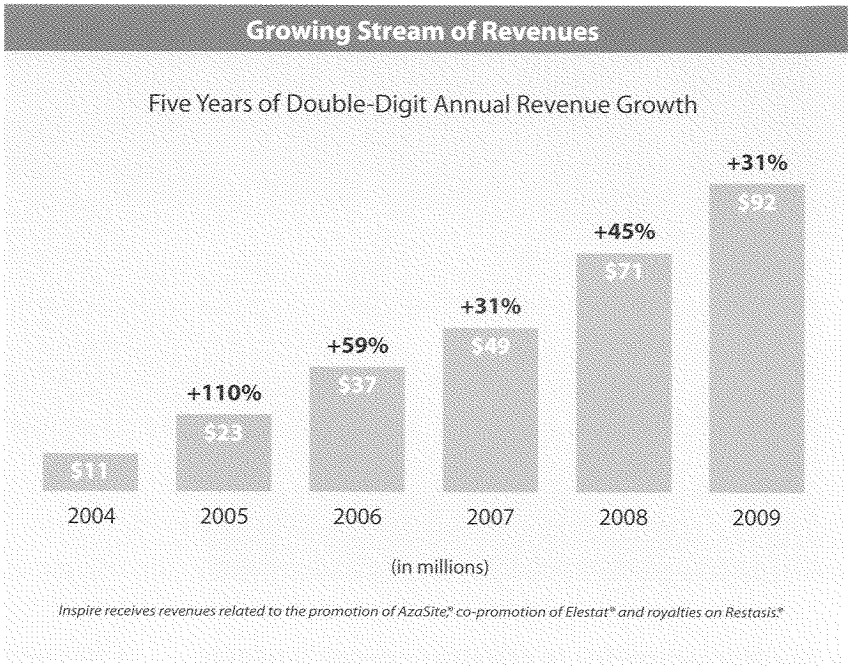
- We enrolled and conducted two exploratory Phase 2 placebo-controlled trials with *AzaSite* towards a potential new indication for blepharitis and also completed a Phase 3 clinical trial with *Prolacria*™ (diquafosol tetrasodium ophthalmic solution) 2% for dry eye. In early 2010, we announced top line results from these trials, which provided useful information in evaluating next steps for the programs, though they did not meet the primary endpoints. We remain interested in the large and growing markets for both dry eye and blepharitis while recognizing that the regulatory and clinical development paths to achieve success are not well defined.
- We completed two Phase 1 clinical trials of INS115644 and INS117548 in glaucoma patients, which provided initial data on safety and potential efficacy to guide next steps.
- We coordinated with our Asian corporate partner, Santen Pharmaceutical Co., regarding DE-089, its formulation of diquafosol tetrasodium. Santen filed for marketing approval of this compound with the Japanese regulatory authority in May 2008. We are following Santen's developments closely in 2010 related to this program.

Delivering Strong Financial Performance

- We posted strong double-digit revenue growth in 2009, despite the challenging economic environment. Total revenues grew 31% over 2008 to $92 million, exceeding our revenue guidance for the year. This revenue growth was driven by strong product sales related to our promotion of *AzaSite* for bacterial conjunctivitis, our co-promotion of *Elestat* for allergic conjunctivitis and royalties we receive based on net sales of *Restasis*® (cyclosporine ophthalmic emulsion) 0.05% for dry eye. The chart on the next page shows how we have successfully generated double-digit annual revenue growth since the initiation of our commercial organization in 2004.
- Operating expenses in 2009 were $130 million, within our budgeted range due to careful expense management and a focused restructuring in the first quarter of 2009. The restructuring enabled us to reduce our cost structure by eliminating preclinical and drug discovery activities, reducing

commercial expenses and refocusing our resources on the development of existing later stage clinical programs and commercially available products.

- As a result of solid revenue growth and tight expense management, we were able to improve our bottom line performance and cash utilization compared to 2008. Our net loss in 2009 decreased by 23% to $40.0 million, or ($0.60) per common share, and our cash burn declined by $14 million to $53 million.
- During 2009, we enhanced the strength of our balance sheet. We ended the year with $129 million in cash and investments, based on a successful public equity offering in August 2009, which generated total proceeds of $115 million.
- We also decreased our outstanding debt balances to a level of $25 million by repaying $18 million during the year.



OTHER DEVELOPMENTS

From a corporate governance perspective, we were very pleased to have Alan Holmer and George Abercrombie join our Board of Directors. Alan has extensive knowledge of the pharmaceutical industry and global markets, which will be important in the evolving regulatory and economic environment, and he is involved in the CF community through his service as Chairman of the Board of the Metropolitan Washington, D.C. Chapter of the Cystic Fibrosis Foundation. George has broad industry experience from senior management roles at Merck & Co., Glaxo Wellcome Inc. and, most recently, Hoffmann-La Roche Inc. that enables him to bring valuable commercial and corporate development and licensing expertise to Inspire.

2010 OBJECTIVES

As we reflect on 2009 and focus on opportunities in 2010 and beyond, we recognize that the next year is a pivotal and potentially transformational time for the Company. Last year's accomplishments, in particular, our robust financial performance and success in raising capital, provide a solid foundation entering 2010. Our team is focused on four major objectives that we believe will help create both near- and long-term shareholder value. These objectives are to:

- Fully **leverage our commercial infrastructure** and enhance overall productivity;
- Drive **excellence in research and development execution;**
- Pursue strategically aligned **corporate development and licensing opportunities;** and
- Deliver **strong financial performance.**

In summary, we are excited about the prospects for Inspire. We have an experienced team of dedicated employees who will be focused but opportunistic in building our business and striving to achieve peak performance and to execute with excellence. We appreciate the support of our key stakeholders – employees, patients, health care providers, partners and stockholders – and look forward to reporting progress to you as the year proceeds and as we continue to build on our **foundations for success**.

Sincerely,

Adrian Adams

Adrian Adams
President and Chief Executive Officer

Foundations For Success

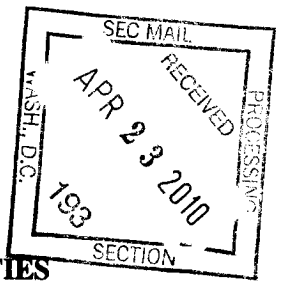
INSPIRE

2009 Form 10-K

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

FORM 10-K

ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934



(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2009

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 No. 000-31135

INSPIRE PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**04-3209022**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
4222 Emperor Boulevard, Suite 200, Durham, North Carolina	**27703-8466**
(Address of Principal Executive Offices)	**(Zip Code)**

(919) 941-9777
(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, $.001 par value	**The Nasdaq Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act: None
(Title of Class)

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 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 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 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 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 ☐ (do not check if a smaller reporting company) Smaller reporting company ☐

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

State the aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter. $235,170,141.

Indicate the number of shares outstanding of each of the Registrant's classes of common stock, as of January 31, 2010.

Class	**Number of Shares**
Common Stock, $.001 par value	82,350,770

Documents incorporated by reference

Document Description	**10-K Part III**
Portions of the Registrant's proxy statement to be filed pursuant to Regulation 14A within 120 days after Registrant's fiscal year end of December 31, 2009 are incorporated by reference into Part III of this report.	Items 10, 11, 12, 13, 14

INSPIRE PHARMACEUTICALS, INC.
2009 FORM 10-K ANNUAL REPORT

TABLE OF CONTENTS

We own or have rights to various trademarks, copyrights and trade names used in our business. *AzaSite*® is a trademark owned by InSite Vision Incorporated. *Restasis*®, *Elestat*® and *Prolacria*™ are trademarks owned by Allergan, Inc. This report also includes trademarks, service marks and trade names of other companies.

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company focused on researching, developing and commercializing prescription pharmaceutical products for ophthalmic and pulmonary diseases. Our goal is to build and commercialize a sustainable portfolio of innovative new products based on our technical and scientific expertise. The most advanced compounds in our clinical pipeline are denufosol tetrasodium for cystic fibrosis and *Prolacria* for dry eye, both of which are in Phase 3 development, and *AzaSite* for blepharitis, which is in Phase 2 development. We receive revenue related to the promotion of *AzaSite* for bacterial conjunctivitis, co-promotion of *Elestat* for allergic conjunctivitis and royalties on *Restasis* for dry eye. Our portfolio of products and product candidates include:

PRODUCTS AND PRODUCT CANDIDATES	THERAPEUTIC AREA/ INDICATION	COLLABORATIVE PARTNER [1]	CURRENT STATUS IN THE UNITED STATES
Products			
AzaSite	Bacterial conjunctivitis	InSite Vision	Promoting
Elestat	Allergic conjunctivitis	Allergan	Co-promoting
Restasis	Dry eye disease	Allergan	Receiving royalty
Product Candidates in Clinical Development			
Denufosol tetrasodium	Cystic fibrosis	None	Phase 3
Prolacria (diquafosol tetrasodium)	Dry eye disease	Allergan; Santen Pharmaceutical	Phase 3 [2]
AzaSite	Blepharitis	InSite Vision	Phase 2
INS115644, INS117548	Glaucoma	Wisconsin Alumni Research Foundation	Phase 1

(1) See "Collaborative Agreements" in this report for a detailed description of our agreements with these collaborative partners.

(2) In January 2010, we announced that our Phase 3 clinical trial (Trial 03-113) did not meet its primary or secondary endpoints. See "Product Candidates in Clinical Development—*Prolacria* (diquafosol tetrasodium)" for additional information on this product candidate.

We were incorporated as a Delaware corporation in October 1993 and commenced operations in March 1995. We are located in Durham, North Carolina, adjacent to the Research Triangle Park.

PRODUCTS

AzaSite

AzaSite (azithromycin ophthalmic solution) 1% is a topical anti-infective, in which azithromycin is formulated into an ophthalmic solution utilizing *DuraSite®*, a novel ocular drug delivery system. Azithromycin is a semi-synthetic antibiotic that is derived from erythromycin and since 1992, has been available via oral administration by Pfizer Inc. under the trade name *Zithromax®*. In April 2007, *AzaSite* was approved by the U.S. Food and Drug Administration, or FDA, for the treatment of bacterial conjunctivitis in adults and children one year of age and older.

In February 2007, we entered into a license agreement with InSite Vision Incorporated, or InSite Vision, pursuant to which we acquired exclusive rights to commercialize *AzaSite* for use in the treatment of human ocular or ophthalmic indications. The license agreement grants us exclusive rights to develop, make, use, market, commercialize and sell *AzaSite* in the United States and Canada. We are obligated to pay InSite Vision royalties on net sales of *AzaSite* in the United States and Canada. See "—Collaborative Agreements—*InSite Vision Incorporated*."

In August 2007, we launched *AzaSite* in the United States and are promoting it to eye care specialists. The manufacture and sale of *AzaSite* is protected in the United States under use and formulation patents, the latest of which expires in March 2019. In addition, the sale of *AzaSite* is also protected in the United States under a use patent that we sub-licensed from Pfizer that expires in November 2018.

Market Opportunity. The U.S. single-entity ocular antibiotic market was approximately $474 million for the 12 months ended December 31, 2009 according to data compiled from IMS Health. Total prescriptions for all branded products in the U.S. ocular antibiotic market were approximately 5.7 million for the 12 months ended December 31, 2009, which was relatively unchanged from the prior year according to data compiled from IMS Health.

Elestat

Elestat (epinastine HCl ophthalmic solution) 0.05% is a topical antihistamine developed by Allergan, Inc., or Allergan, for the prevention of ocular itching associated with allergic conjunctivitis. *Elestat* was approved by the FDA in October 2003 and is indicated for adults and children at least three years old.

We receive co-promotion revenue from Allergan on its U.S. net sales of *Elestat*. When a generic form of *Elestat* or an over-the-counter form of epinastine ophthalmic solution is introduced into the market, our agreement with Allergan to co-promote *Elestat* will no longer be in effect, and our revenues from sales of *Elestat* will be minimal. See "—Collaborative Agreements—*Allergan, Inc.—Elestat*."

Subject to applicable law, competitors are permitted to submit to the FDA an Abbreviated New Drug Application, or ANDA, for a generic version of *Elestat*, due to the expiration of the marketing exclusivity period for *Elestat* provided under the Hatch-Waxman Act on October 15, 2008. Notices have been received from four companies: Apotex, Inc., Cypress Pharmaceutical, Inc., Paddock Laboratories, Inc., and Sandoz Inc., advising that each company filed an ANDA for a generic version of *Elestat*. The date of submission of the first ANDA filing to the FDA Office of Generic Drugs was October 14, 2008, according to the FDA's website (www.fda.gov).

We plan to continue co-promoting and receiving co-promotion revenues on *Elestat* sales during the FDA's review period of these ANDAs. According to an Office of Generic Drugs Update presentation made by Gary Buehler, Director, Office of Generic Drugs, on February 16, 2010, at the GPhA Annual Meeting, the ANDA median approval time for the fiscal period ending September 30, 2009 was approximately 26.7 months. We do not know when the FDA will complete its review of the ANDAs relating to a generic version of *Elestat* and we

do not expect to be notified by any party prior to any approval. However, based upon our assessment, we believe it is likely that a generic form of epinastine may be launched in the second half of 2010. See the risk factor entitled— "*When a generic form of Elestat or an over-the-counter form of epinastine ophthalmic solution is introduced into the market, our agreement with Allergan to co-promote Elestat will no longer be in effect, and our revenues from sales of Elestat will be minimal*"—for further discussion of the risk related to the ANDA filings.

Restasis

Restasis (cyclosporine ophthalmic emulsion) 0.05% is the first approved prescription product in the United States for the treatment of dry eye disease. It is indicated to increase tear production in adults and children at least 16 years old whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca, or dry eye disease. *Restasis* was approved by the FDA in December 2002, and Allergan launched the product in the United States in April 2003.

In June 2001, we entered into an agreement with Allergan to develop and commercialize our product candidate, *Prolacria* (diquafosol tetrasodium), for the treatment of dry eye disease. The agreement also provides that Allergan pay us royalties on net sales of *Restasis*. See "—Collaborative Agreements—*Allergan, Inc.—Restasis and Prolacria.*"

Following the expiration of a use patent in August 2009, the manufacture and sale of *Restasis* is protected in the United States by a formulation patent that expires in May 2014.

Market Opportunity: Other than *Restasis*, the current treatments for dry eye disease in the eight major international prescription pharmaceutical markets consist of artificial tear solutions and lubricant eye drops. Dry eye disease is associated with aging, environmental factors, autoimmune disorders and various medications. According to Allergan, dry eye disease affects an estimated 21 million people in the United States. For the years ended December 31, 2009, 2008 and 2007, Allergan has recognized approximately $523 million, $444 million and $345 million, respectively, of revenue from net sales of *Restasis*.

For a more detailed discussion of the risks associated with these products, please see the Risk Factors located elsewhere in this report.

PRODUCT CANDIDATES IN CLINICAL DEVELOPMENT

Denufosol tetrasodium for the treatment of cystic fibrosis

Overview. We are developing denufosol tetrasodium as an inhaled product candidate for the treatment of cystic fibrosis. Denufosol tetrasodium is a first-in-class ion channel regulator that addresses the underlying ion transport defect in the lungs of patients with cystic fibrosis. Denufosol is designed to enhance airway hydration and mucociliary clearance through receptor-mediated mechanisms that increase chloride secretion, inhibit sodium absorption and increase ciliary beat frequency. These integrated pharmacological actions are important to restoring airway clearance, maintaining lung function, and potentially delaying the progression of cystic fibrosis lung disease. We believe that our product candidate could be the first FDA-approved product that mitigates the underlying defect in the airways of patients with cystic fibrosis. If approved, we expect denufosol to be an early intervention therapy for cystic fibrosis. This product candidate has been granted orphan drug status and fast-track review status by the FDA, and orphan drug status by the European Medicines Agency.

The manufacture and sale of denufosol tetrasodium is protected in the United States under patents that have claims to the drug substance, the formulation, and method of use that expire in February 2017, subject to any applicable patent restoration that may extend protection up to an additional five years from the date of expiration of the applicable patent, if any, for which restoration is sought.

Development Status

TIGER 1: Our first Phase 3 clinical trial, TIGER-1 (Trial 08-108), with denufosol tetrasodium inhalation solution for the treatment of cystic fibrosis was a 24-week, double-blind, placebo-controlled, randomized clinical trial comparing 60 mg of denufosol to placebo, administered three-times daily by jet nebulizer, in 352 patients with mild cystic fibrosis lung disease (FEV_1 (Forced Expiratory Volume in One Second) (in liters) ≥ 75% predicted normal) at clinical centers across North America. This portion of the clinical trial was followed by a 24-week denufosol-only open-label extension, or OLE.

In June 2008, we announced top-line results from the 24-week placebo-controlled portion of the clinical trial. The clinical trial demonstrated statistical significance for its primary efficacy endpoint, which was the change in FEV_1 from baseline at the clinical trial endpoint (at 24 weeks or last observation carried forward). Patients treated with denufosol had a statistically significant improvement in FEV_1 compared to placebo (45 milliliter treatment group difference in adjusted means, p = 0.047). On average, patients on denufosol improved in FEV_1 relative to baseline whereas patients on placebo remained essentially unchanged. Secondary endpoints were also evaluated during the placebo-controlled portion of TIGER-1. There was a trend in differences in $FEF_{25\%-75\%}$ (Forced Expiratory Flow 25%-75%), a measure of small airway function, favoring denufosol over placebo (87.5 milliliters/second treatment group difference, p = 0.072).

In October 2008, we presented new data at the North American Cystic Fibrosis Conference which indicate that patients who continued to receive denufosol for an additional 24 weeks during the OLE experienced a progressive improvement in FEV_1. Those patients who received denufosol for 48 weeks during TIGER-1 experienced a mean change from baseline in FEV_1 of 115 ml at the end of the OLE, almost a two-and-a-half fold increase compared to the initial 48 ml increase at the end of the 24-week placebo-controlled portion of the trial.

The patients who crossed over from placebo to denufosol at Week 24 also experienced improvements in FEV_1 when receiving denufosol during the OLE. In terms of observed means, these patients had a 78 ml increase from baseline, compared to a 16 ml increase at the end of the 24-week placebo-controlled portion of the trial. This differs from the 3 ml adjusted mean for placebo at the 24-week study endpoint which also accounted for discontinuations.

A total of 315/352 (89%) patients completed the 24-week placebo-controlled phase of TIGER-1 and had the option to participate in the OLE phase in which all patients received denufosol for an additional 24 weeks. All of the patients but one (n=314) entered the OLE extension. The objective of the OLE phase was to evaluate the long-term safety of denufosol treatment among cystic fibrosis patients with FEV_1 ≥ 75% predicted normal. In the TIGER-1 trial, there was no evidence of adverse effects on growth, clinical laboratory values or vital sign assessments with long-term denufosol treatment. Denufosol was well-tolerated over 48 weeks of dosing in the TIGER-1 trial.

The retention rate during the OLE phase was approximately 96%, with 302 patients completing the full 48 weeks. Twelve patients withdrew during the OLE phase, with only four withdrawals related to Adverse Events, or AEs. In the OLE phase, the most commonly reported AEs, which included cough, condition aggravated and productive cough, were similar to those reported during the placebo-controlled phase. The incidence of Serious Adverse Events, or SAEs, in the OLE phase was under 20% and the majority of SAEs were pulmonary exacerbations.

In TIGER-1, there were two definitions of pulmonary exacerbations in the protocol. Based on the primary protocol definition of an exacerbation as a patient experiencing at least four out of 12 defined signs and symptoms regardless of treatment, the frequency of pulmonary exacerbations was 23% in both the placebo-controlled phase and the OLE phase. Based on the secondary protocol definition of an exacerbation as a patient requiring treatment with IV antibiotics for a respiratory sign or symptom, the frequency of pulmonary exacerbations was 8% in the placebo-controlled phase and 13% in the OLE phase.

TIGER 2: In February 2008, we initiated patient enrollment in TIGER-2 (Trial 08-110), our second planned pivotal Phase 3 clinical trial, and in July 2008, we announced modifications to the clinical protocol for this ongoing clinical trial. As modified, the TIGER-2 clinical trial is a 48-week, double-blind, placebo-controlled, randomized clinical trial comparing 60 mg of denufosol to placebo, administered three-times daily by jet nebulizer, in approximately 450 patients with FEV_1 greater than or equal to 75% and less than or equal to 110% of predicted normal. The primary efficacy endpoint is the change from baseline in FEV_1 (in liters) at the 48-week trial endpoint. Secondary endpoints include other lung function parameters, pulmonary exacerbations, requirements for concomitant cystic fibrosis medications and health related quality of life. Patients aged five years and older are eligible for enrollment. The use of standard cystic fibrosis maintenance therapies is permitted during the trial. Hypertonic saline is not permitted to be used by those patients enrolled in the clinical trial.

We have approximately 100 participating clinical trial sites across the United States, Canada, Australia and New Zealand and completed patient enrollment in November 2009. Top-line results from this clinical trial are expected in the first quarter of 2011.

Additionally, any patient who has successfully completed TIGER-2 may elect to participate in a follow-on, open-label denufosol-only trial (Trial 08-114) which will enable patients to continue receiving denufosol for up to 3 additional years. The original length of this extension study was 48 weeks, but this was recently extended to 3 years to assess the potential disease-modifying effects of extended denufosol treatment on lung function over time. To date, more than 80% of the patients who have completed TIGER-2 have elected to enroll in this long-term study.

Assuming the results of TIGER-2 are positive, that we subsequently file a New Drug Application, or NDA, for denufosol with the FDA and that the FDA approves such NDA, we are targeting a potential U.S. commercial launch for denufosol in the 2012 timeframe.

Other: In 2006, we completed a 52-week inhalation toxicology study in one animal species, and have submitted the final study report to the FDA. There were no signs of pulmonary or systemic toxicity at doses well above the Phase 3 clinical dose. In 2009, we completed the required two-year inhalation carcinogenicity study in rats and the final study report confirms that there was no evidence of a carcinogenic effect with denufosol.

Estimated subsequent costs necessary to submit an NDA for denufosol for the treatment of cystic fibrosis are projected to be in the range of $21 million to $28 million. This estimate includes completing TIGER-2 as well as conducting any additionally required toxicology studies and other ancillary studies, manufacturing denufosol for clinical trials, producing qualification lots consistent with current Good Manufacturing Practices, or cGMP, standards, salaries for development personnel, other unallocated development costs and regulatory preparation and filing costs. These costs do not include the costs of pre-launch inventory and any product approval milestones payable to Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT. See—"Collaborative Agreements—*Cystic Fibrosis Foundation Therapeutics, Inc.*" These costs are difficult to project and actual costs could be materially different from our estimate. For example, clinical trials and any other required studies may not proceed as planned, results from ongoing or future clinical trials may change our planned development program, additional Phase 3 clinical trials may be necessary and an anticipated NDA filing could be delayed.

In addition to the activities and costs necessary to submit an NDA for denufosol, we are initiating pre-launch and franchise development activities, including conducting market research, developing manufacturing plans, and expanding our clinical and scientific database on denufosol beyond the TIGER-1 and TIGER-2 pivotal trials. More specifically, these activities would include the extension study (Trial 08-114) discussed above and development of a secondary supplier of denufosol. We expect the costs of these activities to be significant and will include approximately $8 million in remaining milestone payments due under our technology license agreement with Yamasa Corporation. See "—Manufacturing and Supply—*Yamasa Corporation.*"

We currently plan to retain commercial rights for denufosol for the treatment of cystic fibrosis in North America. We continue to seek a corporate partner to develop and commercialize this product candidate outside of North America.

Market Opportunity. The current commercially available therapeutic approaches to address cystic fibrosis mainly treat the complications of the disease and are aimed at reducing respiratory infections and breaking up thickened mucous secretions that cause airflow obstruction and harbor bacteria. For example, *TOBI* is an inhaled antibiotic that treats lung infections and *Pulmozyme* is an inhaled protein that breaks up excessive DNA in mucus that reduces the thickness and tackiness of the respiratory secretions. While both products are approved for the management of cystic fibrosis, neither product is designed to address the underlying ion-transport defect, which results in dehydrated mucus and severely impaired mucociliary clearance.

According to the U.S. Cystic Fibrosis Foundation, there are approximately 30,000 cystic fibrosis patients in the United States, and approximately 70,000 cystic fibrosis patients worldwide. Based on data compiled and reported by IMS Health as of December 31, 2009, annual sales in the United States of the two prescription pharmaceutical products to treat cystic fibrosis lung disease, *Pulmozyme* and *TOBI*, were approximately $328 million and $242 million, respectively, and represented approximately two-thirds of annual world-wide sales of these two products.

Prolacria (diquafosol tetrasodium) for the treatment of dry eye disease

Overview. Diquafosol tetrasodium is a dinucleotide which functions as an agonist at the $P2Y_2$ receptor and is being developed for the treatment of dry eye disease. *Prolacria*, the proposed U.S. tradename for diquafosol tetrasodium ophthalmic solution 2%, is designed to stimulate the release of three components of natural tears—mucin, lipids and fluid. The manufacture and sale of *Prolacria* is protected in the United States under drug substance and formulation patents that expire in July 2016, as well as under use patents that expire in February 2017, subject to any applicable patent restoration that may extend protection up to an additional five years from the date of expiration of the applicable patent, if any, for which restoration is sought.

Under our agreement with Allergan, we are responsible for the development of *Prolacria* in the United States, and Allergan is responsible for the commercialization of *Prolacria* in the United States. If we receive FDA approval and *Prolacria* is launched, we expect to co-promote this product. Pursuant to this agreement, Allergan is responsible for obtaining regulatory approval and for commercializing diquafosol tetrasodium in Europe and elsewhere globally with the exception of Asia. See "—Collaborative Agreements—*Allergan, Inc.—Restasis and Prolacria.*"

Development Status. In June 2003, we filed an NDA with the FDA for *Prolacria* for the treatment of dry eye disease. We received approvable letters from the FDA in December 2003 and December 2005. In September 2008, we submitted a clinical protocol and request for Special Protocol Assessment, or SPA, to the FDA for a pivotal Phase 3 environmental trial with *Prolacria*. During 2009, we reached agreement with the FDA on the design of a Phase 3 clinical trial for *Prolacria,* and completed the trial.

In January 2010, we announced that this Phase 3 clinical trial (Trial 03-113) did not meet its primary endpoint ($p = 0.526$) or its secondary endpoint ($p = 0.368$). Given the complexity of this program and the large database of information we have, we are working closely with our partner, Allergan, to determine potential next steps for the program.

Due to the uncertainty of the future of this program, we are currently unable to reasonably project the future dates and costs associated with additional clinical trials or other work which would be necessary to amend our NDA submission for *Prolacria* and resubmit the application for commercial approval in the United States.

Our partner, Santen Pharmaceutical Co., Ltd., or Santen, is currently developing a different formulation of diquafosol tetrasodium, which it refers to as DE-089, in Japan. Our agreement with Santen allows Santen to develop diquafosol tetrasodium for the therapeutic treatment of ocular surface diseases, such as dry eye disease, in Japan and nine other Asian countries, and provides for certain milestone payments to be paid to us upon achievement of development milestones by Santen. In May 2008, Santen filed an application for manufacturing and marketing approval of DE-089 with the Japanese Ministry of Health, Labor, and Welfare (the Japanese equivalent of the FDA), which is pending review. See "—Collaborative Agreements—*Santen Pharmaceutical Co., Ltd.*"

AzaSite for the treatment of blepharitis

Overview. Blepharitis is an ocular disease characterized by inflammation of the lid margin that is common, complex, and has a multi-factorial etiology. Blepharitis coexists with other common ocular surface conditions and is often under-diagnosed and misdiagnosed in general clinical practice. Blepharitis can be subdivided into two categories: anterior and posterior blepharitis. Although they are distinct diseases, they can overlap. Anterior blepharitis is generally associated with the presence of bacteria, lid debris and/or sebaceous gland activity and is most often an acute disease. Posterior blepharitis is almost always associated with dysfunctional meibomian glands or altered meibomian gland secretions and is generally considered a chronic disease.

Our market research and input from eye care specialists suggests that blepharitis is an under-diagnosed and under-treated disease. Survey data published in The Ocular Surface and funded by Inspire indicated that 15 percent of adults reported having at least one of the three symptoms that clinicians associate with anterior blepharitis at least half of the time in the previous 12 months. Based on the overall U.S. adult population of 232 million, this implies potentially as many as 34 million adults might have suffered from some form of blepharitis over such time frame. Currently, there are no FDA-approved prescription pharmaceutical products indicated for the treatment of this disease. Patients currently manage the acute and often chronic effects of blepharitis with the use of warm compresses, lid hygiene, topical antibiotic ointments and, when exacerbated, with topical steroids or oral antibiotics.

Development Status. During 2008, we conducted a series of Phase 4 clinical trials with *AzaSite* evaluating the safety and efficacy of *AzaSite* in ocular conditions, such as blepharitis. In late 2008, we sought input from numerous medical experts and evaluated our Phase 4 data along with market research on the prevalence and awareness of the disease to evaluate *AzaSite's* potential opportunity as it relates to the treatment of blepharitis. In addition, we had preliminary discussions with the FDA on potential regulatory pathways. Based on preliminary information gathered, we decided to pursue a Phase 2 program to study *AzaSite* for the treatment of blepharitis.

In May 2009, we initiated Phase 2 work which consisted of two randomized, vehicle-controlled clinical trials that enrolled approximately 600 patients with anterior blepharitis. Trial 044-101 included a two-week treatment period with a two-week follow-up period and Trial 044-102 included a four-week treatment period with a four-week follow-up period. Patients were randomized to *AzaSite* or the *DuraSite* vehicle and received one drop in each eye twice-a-day for the first two days, then one drop in each eye daily for the remainder of the treatment period. All patients in the trials performed lid hygiene using commercially available lid scrubs once daily for the duration of the trials.

In March 2010, we announced the results of these two trials. In the four-week trial, improvements for *AzaSite* compared to vehicle were achieved for a number of blepharitis signs and symptoms at various time points with p-values ≤ 0.05, but statistical significance was not achieved for the primary endpoint of mean lid margin hyperemia. In the two-week trial, there were no statistically significant improvements for *AzaSite* compared to vehicle, including for the primary endpoint of clearing of lid debris. In both trials, the *AzaSite* treatment group and the vehicle treatment group showed statistically significant improvements relative to baseline for all measured signs and symptoms of blepharitis. Additionally, *AzaSite* was well-tolerated in both trials.

We will conduct additional clinical work to continue pursuing a potential indication for treatment of anterior and posterior forms of blepharitis.

Given the limited data available and the early stage of development of this program, we are currently unable to reasonably project the future dates and costs associated with clinical trials or a prospective NDA filing for this program. Additionally, since there are no prescription pharmaceutical products indicated for the treatment of blepharitis, we are unable to provide U.S. market opportunity data.

Glaucoma product candidates

Overview. In November 2004, we licensed technology for use in developing and commercializing new treatments for glaucoma from Wisconsin Alumni Research Foundation, or WARF. See "—Collaborative Agreements—*Wisconsin Alumni Research Foundation.*" In relation to this technology, we are evaluating new and existing compounds that are active in disrupting the acto-cytoskeleton of the trabecular meshwork as potential treatments for glaucoma. Our scientific hypothesis is that the mechanism of action may result in reduction of intraocular pressure, or IOP, by affecting the primary outflow pathway for aqueous humor.

Development Status. In the first quarter of 2007, we initiated a Phase 1 proof-of-concept placebo-controlled, dose-ranging clinical trial (Trial 032-101) for INS115644, the first compound in a series of compounds, in glaucoma patients to evaluate the safety and tolerability of INS115644, as well as changes in IOP. In September 2008, we initiated a Phase 1 proof-of-concept placebo-controlled, dose-ranging clinical trial (Trial 037-101) for a second compound, referred to as INS117548, to evaluate the safety, tolerability and IOP-lowering effects of INS117548 in approximately 80 subjects with early stage glaucoma or ocular hypertension.

In September 2009, we announced top-line results of these trials. In Trial 032-101 with INS115644, a Latrunculin B formulation, we observed dose-dependent IOP-lowering effects and the compound was well-tolerated. Trial 037-101 with INS117548, which is one of a series of Rho kinase molecules we have developed, showed mild IOP-lowering effects but had some dose-related tolerability issues, specifically with ocular discomfort such as burning and stinging. We are in the process of evaluating next steps for the overall glaucoma program, based on our clinical and preclinical data, expert opinions and resource availability.

Due to the uncertainty of the future of this program, and given the limited data available and the early stage of development of this program, we are currently unable to reasonably project the future dates and costs associated with clinical trials or a prospective NDA filing for either of these product candidates.

Market Opportunity. The current market for treatment of glaucoma, the largest market in ophthalmic pharmaceuticals, is approximately $2.2 billion in annual sales in the United States based on data compiled and reported by IMS Health as of December 31, 2009.

For a discussion of the risks associated with our development programs, please see the Risk Factors located elsewhere in this report.

Additional information about the costs and expenses associated with all of our research and development programs is discussed below in "Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations—Years Ended December 31, 2009, 2008 and 2007—Costs and Expenses."

Collaborative Agreements

Allergan, Inc.—Elestat

In December 2003, we entered into an agreement with Allergan to co-promote *Elestat* in the United States. Under the agreement, we have the responsibility for promoting and marketing *Elestat* to ophthalmologists, optometrists and allergists in the United States and paying the associated costs. We receive co-promotion revenue

from Allergan on its U.S. net sales of *Elestat*. Allergan records sales of *Elestat* and is responsible for supply chain management, managed health care, customer order processing and regulatory compliance, as well as any international marketing and selling activities.

The *Elestat* co-promotion agreement provides that unless earlier terminated, the term of such agreement will be in effect until the earlier of (i) the approval and launch of the first generic epinastine product after expiration of the FDA exclusivity period covering *Elestat* in the United States, or (ii) the approval and launch of the first over-the-counter epinastine product after expiration of the listing of *Elestat* in the FDA's Orange Book. Following the termination of such co-promotion agreement, we will no longer have rights to co-promote *Elestat*. We will be entitled to receive post-termination payments from Allergan, based on any remaining net sales of *Elestat* for a period of 36 months. During the three successive 12-month periods immediately following the termination of the agreement, Allergan will be obligated to pay to us 20%, 15% and 10%, respectively, on any net sales of *Elestat* in the United States. See "—Products—*Elestat*" for a discussion of the filing of ANDAs by various pharmaceutical companies relating to generic forms of *Elestat*.

Either Allergan or we may terminate the agreement in the event of a material breach of the agreement by the other or in the event of the other's insolvency. Allergan can terminate the agreement upon a change of control where we become an affiliate of a direct competitor of Allergan as that term is defined in the agreement. We can terminate the agreement in the event that *Elestat* is withdrawn from the market for more than 90 days.

Allergan, Inc.—Restasis and Prolacria

In June 2001, we entered into a joint license, development and marketing agreement with Allergan to develop and commercialize our product candidate, *Prolacria*, for the treatment of dry eye disease. The agreement also provided us with revenue on net sales of Allergan's *Restasis*.

Under the terms of the agreement, Allergan obtained an exclusive license to develop and commercialize *Prolacria* worldwide, with the exception of Japan and nine other Asian countries covered by our agreement with Santen. In return, we are entitled to receive revenue from Allergan on net sales of *Restasis* and *Prolacria*, if any, worldwide, excluding most larger Asian markets. Under this agreement, we have received up-front and milestone payments of $11 million related to our development of *Prolacria* and will be entitled to receive up to an additional $28 million in milestone payments assuming the successful completion of all remaining milestones under this agreement. If we receive FDA approval and *Prolacria* is launched, we expect to begin to co-promote this product in the United States.

We have established a joint development committee with Allergan to oversee the joint development program and a joint commercialization committee to establish the broad strategies and manage the relationship. Under the terms of the agreement, we provide bulk active drug substance while *Prolacria* is in development and Allergan is responsible for obtaining or manufacturing all of its bulk active drug substance requirements for commercial supply of the product.

We are responsible for conducting, in collaboration with Allergan, the Phase 3 clinical trials needed to file a U.S. NDA for *Prolacria*. Allergan is responsible for all other development activities under the agreement, including all development and regulatory activities needed for potential approval outside the United States and in its territories, and for ex-U.S. regulatory submissions, filings, and approvals relating to products. In addition, Allergan is responsible for all commercial costs except for the cost of our sales force in the United States. Allergan is required to use commercially reasonable efforts to conduct these development activities, seek ex-U.S. regulatory approvals and market and sell *Prolacria*.

The revenue that we receive on the net sales of *Restasis* is based upon a percentage of net sales of Restasis in the United States, and upon a percentage of net sales of *Restasis* outside the United States, except in Japan and nine other Asian countries covered by our agreement with Santen.

In December 2008, we amended our agreement with Allergan such that we ceased co-promoting *Restasis* as of December 31, 2008. Notwithstanding the fact that we are no longer co-promoting *Restasis*, Allergan remains obligated to pay us royalties in relation to sales of *Restasis* at the rates in effect prior to the December 2008 amendment.

Unless earlier terminated pursuant to other terms of the agreement, the agreement will expire as to each product (*Restasis* or *Prolacria*, as the case may be) in each applicable country on the later of (i) the 10th anniversary of the first commercial sale of such product in the applicable country, or (ii) the date on which the sale of such product ceases to be covered by any claim of any applicable Inspire or Allergan patent. The agreement will expire in its entirety upon the expiration of the agreement with respect to all products in all countries as described in the previous sentence. Either Allergan or we may terminate the agreement in the event of a material breach of the agreement. In addition, we have the right to terminate the agreement by giving 180 days prior notice if we determine, subject to the joint commercialization committee's review and arbitration, that Allergan has not made reasonably sufficient progress in the commercialization of our product. If Allergan breaches the agreement, becomes insolvent or we terminate for failure to make progress with the commercialization of our product, Allergan's license will terminate and Allergan must provide us with all data and information relating to our product and must assign or permit us to cross-reference all regulatory filings and approvals.

In the event that the joint development committee decides to terminate the development program for *Prolacria*, and any other Inspire product under development pursuant to the agreement, and we do not within six months of the termination of the development program fulfill our obligations under the co-promotion provisions for *Restasis*, including providing 20% of the budgeted sales force for *Restasis,* the royalty that we receive on net sales of *Restasis,* both with respect to sales in the United States and elsewhere, will be reduced by 30%.

Cystic Fibrosis Foundation Therapeutics, Inc.

In October 2002, we entered into a study funding agreement with the CFFT, a non-profit drug development affiliate of the Cystic Fibrosis Foundation, for the funding of one Phase 2 clinical trial for denufosol for the treatment of cystic fibrosis. Under the agreement, the CFFT provided the majority of funding of external costs for one Phase 2 clinical trial of denufosol, which we completed in April 2004, in exchange for post-commercialization development and sales milestone payments. If denufosol ultimately receives FDA approval for the treatment of cystic fibrosis, we would be obligated to pay a development milestone to the CFFT, calculated as a multiple of the clinical trial costs incurred by the CFFT. In addition, we would be obligated to pay a sales milestone if the product candidate achieves a specified aggregate sales volume in the first five years following product approval. The development milestone is currently estimated to be approximately $12 million, payable over five years, and the sales milestone would be an additional $4 million, payable over two years. The agreement will terminate no later than the expiration of all payment obligations under the agreement. Either the CFFT or we may terminate the agreement if the other materially breaches the agreement.

InSite Vision Incorporated

In February 2007, we entered into a license agreement with InSite Vision pursuant to which we acquired exclusive rights to commercialize *AzaSite*, as well as other potential topical anti-infective products containing azithromycin as the sole active ingredient for use in the treatment of human ocular or ophthalmic indications. The license agreement also grants us exclusive rights to develop, make, use, market, commercialize and sell each product in the United States and Canada. We are currently responsible for all regulatory obligations and strategies relating to the further development and commercialization of a product in the United States and Canada.

Pursuant to the license agreement, we paid InSite Vision an upfront license fee of $13.0 million and an additional $19.0 million milestone related to FDA approval of *AzaSite*. In addition, we paid a 20% royalty for the first two years of commercialization and in July 2009 began paying a 25% royalty on net sales of *AzaSite* in the

United States and Canada, which will continue for the duration of the agreement. We are obligated to pay royalties under the agreement for the longer of (i) 11 years from the launch of the subject product and (ii) the period during which a valid claim under a patent licensed from InSite Vision covers a subject product. Under the terms of the agreement, our obligation to pay royalties to InSite Vision is subject to pre-determined minimum annual royalty payments. The determination of whether or not we will owe any such payments is based upon the amount of royalties accrued over a 12-month royalty period. There are five successive 12-month minimum royalty periods, the second of which commenced on October 1, 2009.

Contemporaneously with the license agreement, InSite Vision entered into an exclusive license agreement with Pfizer for certain Pfizer patent rights relating to the treatment of ocular infection with azithromycin for certain products. Under the terms of our license agreement with InSite Vision, we obtained from InSite Vision a sublicense to such Pfizer patent rights, in addition to the license to the InSite Vision patent rights, subject to certain limitations. Also, Inspire and Pfizer entered into a related agreement that provides for the continuation of our sublicense rights under the Pfizer patent rights upon a termination of the license agreement between InSite Vision and Pfizer. The agreement between us and Pfizer also provides an opportunity to cure any breaches by InSite Vision of the license agreement between InSite Vision and Pfizer and the opportunity to maintain and enforce such Pfizer patent rights under certain circumstances.

Santen Pharmaceutical Co., Ltd.

In December 1998, we entered into a development, license and supply agreement with Santen for the development of diquafosol tetrasodium for the therapeutic treatment of ocular surface diseases, such as dry eye disease, in Asia. Under the agreement, we granted Santen an exclusive license to develop and market diquafosol tetrasodium for ocular surface diseases in Japan, China, South Korea, the Philippines, Thailand, Vietnam, Taiwan, Singapore, Malaysia and Indonesia.

We established a coordinating committee to review and evaluate Santen's progress in the development and commercialization of potential products. Santen is responsible for all development, regulatory submissions, filings and approvals, and all marketing of potential products in its territory. We are obligated to supply Santen with all its requirements of diquafosol tetrasodium in bulk drug substance form for all preclinical studies, clinical trials and commercial requirements at agreed-upon prices. However, we do not have manufacturing expertise or capability, and we do not have an agreement with any third party for the manufacture of diquafosol tetrasodium in bulk drug substance form for the commercial requirements of Santen's product, if approved. See below and "Risk Factors—*The third-party vendor that manufactures denufosol and the API related to both Prolacria and Santen's DE-089 does not have the capacity to manufacture the projected commercial quantities of API for these products, if any is approved.*"

Under the terms of the agreement, we received an up-front equity investment of $1.5 million in exchange for shares of our preferred stock in December 1998, that were subsequently converted into shares of our common stock. We have received total milestone payments of $3.0 million based on the achievement of certain regulatory work and the completion of Phase 3 clinical testing of diquafosol tetrasodium in Japan by Santen, which Santen refers to as DE-089. If all milestones are achieved, we could receive up to an additional $1.75 million. We are eligible to receive royalties on net sales of DE-089 if it is approved for commercialization and launched in Santen's licensed territories.

The agreement will terminate when all patents licensed under the agreement have expired. Either Santen or we may terminate the agreement if the other materially breaches the agreement. In addition, we have the right to terminate the agreement at any time if we determine, subject to the coordinating committee's review and arbitration, that Santen has not made reasonably sufficient progress in the development or commercialization of potential products. If Santen breaches the agreement, or if we terminate the agreement because Santen has not made sufficient progress, Santen's license will terminate. Santen will provide us with all data and information relating to our products, and will assign or permit us to cross-reference all regulatory filings and approvals. If we

are unable to supply Santen with the API for its DE-089 product, Santen may elect to manufacture (or have manufactured) the quantity of API that we fail to supply or to assume full responsibility for supply of the API. In such event, Santen will receive a manufacturing license from us. In the event that we are in material breach of our material contractual obligations regarding supply of API, other remedies available under law or in equity will apply.

Wisconsin Alumni Research Foundation

In November 2004, we licensed technology for use in developing and commercializing new treatments for glaucoma from WARF. Under the terms of the agreement, we paid an upfront licensing payment of $150,000 in 2004 upon execution of the agreement and a $50,000 milestone payment related to the filing of an Investigational New Drug Application, or IND, for our glaucoma program in 2006. We are obligated for additional contingent payments of up to an aggregate of $1.8 million upon the achievement of development milestones, and royalties on sales of any regulatory approved product utilizing the licensed patents.

We will design and fund all future research, development, testing, regulatory filings and potential marketing activities related to any product candidate under development or product developed from the license. Unless terminated earlier, the agreement will expire on a country-by-country basis upon the expiration of the patents in such country. The U.S. government may have limited rights in some of this patented technology. WARF may terminate the license if we fail to make timely payment of any amount due to WARF under the agreement or commit a material breach of any material covenant contained in the agreement, subject to our right to cure.

Research and Development

Since our inception, we have made substantial investments in research and development. During the years ended December 31, 2009, 2008 and 2007, our research and development expenses were $51.1 million, $44.6 million and $53.4 million, respectively. In February 2009, we eliminated our early preclinical and molecule discovery activities and refocused our resources on the development of existing later-stage clinical programs and commercially available products.

In addition to internal resources, we collaborate with external contract research organizations that allow us to perform development activities, including toxicology, pharmacokinetics, toxicokinetics, and other studies required for NDA regulatory submissions, with a limited number of staff. We routinely present our scientific research at eye care and pulmonary conferences and in peer-reviewed publications.

For more information about our research and development costs and expenses, see "Management's Discussion and Analysis of Financial Conditions and Results of Operations—Research and Development Expenses."

Sales and Marketing

We currently employ approximately 90 territory managers to provide us with national U.S. sales coverage for *AzaSite* and *Elestat*. We also have marketing, managed care, training and operation groups to support our commercialization efforts. Our sales and marketing organization focuses its promotional activities for *AzaSite* and *Elestat* on eye care specialists.

We intend to establish corporate partnering, licensing or other arrangements for the marketing and sale of selected product candidates that we develop, especially outside of North America. We do not intend to develop commercial operations outside of North America.

We believe our commercial operations provides us with the foundation to leverage opportunities to market and sell other products we are developing, or products that we may in-license or otherwise acquire, and to maximize their commercial value in the United States.

Compliance

We conduct our business in an ethical, fair, honest and lawful manner. We act responsibly, respectfully and with integrity in our relationships with patients, health care professionals, providers, governments, regulatory entities, customers, stockholders, suppliers and vendors.

We have designated a Chief Compliance Officer who reports to the Chief Executive Officer and the Chairperson of the Audit Committee of the Board of Directors. Among other duties, this officer oversees compliance training, education, auditing and monitoring; enforces disciplinary guidelines for any infractions of our Comprehensive Compliance Program; implements new policies and procedures; responds to any detected issues; and undertakes corrective action procedures. The Chief Compliance Officer provides updates to senior management, the Audit Committee of the Board of Directors, and to the full Board of Directors. Our controls address compliance matters relating to requirements and entities that govern public pharmaceutical companies including, but not limited to the following: federal and state law, such as the Sarbanes-Oxley Act of 2002 and the U.S. Foreign Corrupt Practices Act of 1977; NASDAQ listing requirements; the Financial Industry Regulatory Authority; the Securities and Exchange Commission; the Food and Drug Administration; the United States Department of Health and Human Services; and the Office of Inspector General, along with voluntary industry standards developed by the Pharmaceutical Research and Manufacturers of America. Our standard operating procedures are designed to provide a framework for corporate governance in accordance with ethical standards and legal best practices. Our codes and policies that have been implemented include, but are not limited to, Code of Conduct and Business Ethics; Whistleblower Policy; and Code of Conduct: Promotional Interactions with Health Care Professionals.

Manufacturing and Supply

We rely on single source manufacturers for our commercial products and product candidates. Allergan is responsible for the manufacturing of both *Restasis* and *Elestat* and relies on single source manufacturers for the active pharmaceutical ingredients, or APIs, in both products. We rely on InSite Vision for supply of the active pharmaceutical ingredient for *AzaSite*, which InSite Vision obtains from a single source manufacturer. We are responsible for the remaining finished product manufacturing of *AzaSite*, for which we rely on a single source manufacturer. Additionally, we rely upon a single third party to provide distribution services for *AzaSite.*

We rely upon one vendor as the sole manufacturer of the supply of active pharmaceutical ingredients for both *Prolacria* and denufosol; however, we have initiated development of a secondary supplier for denufosol. See "Risk Factors—*Reliance on a single party to manufacture and supply either finished product or the bulk active pharmaceutical ingredients for a product or product candidates could adversely affect us*" and "*The third-party vendor that manufactures denufosol and the API related to both* Prolacria *and Santen's DE-089 does not currently have the capacity to manufacture the projected commercial quantities of API for all these products, if approved.*"

We conduct qualification and routine audits of our contract manufacturers. These contract manufacturers are identified in our regulatory agency filings, such as with the FDA, and are subject to regulatory agency inspections. We also attempt to stay informed on the financial condition of contract manufacturers and their status with regulatory agencies.

The manufacture of our products and product candidates is based, in part, on technology that we believe to be proprietary to our contract manufacturers or our collaborative partners. Such manufacturers may not abide by the limitations or confidentiality restrictions in agreements with us. In addition, any such manufacturer may develop process technology related to the manufacture of our compounds that such supplier owns either independently or jointly with us. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have our products manufactured using such technology.

Catalent Pharma Solutions

In September 2007, we entered into a long term manufacturing services agreement with Catalent Pharma Solutions, LLC, or Catalent, for the manufacture of the finished product *AzaSite*, pursuant to which Catalent agreed to manufacture *AzaSite* to Inspire's specifications for a period of six years. Under the agreement, we agreed to purchase from Catalent on an annual basis a specified minimum number of units (each unit consists of 2.5 milliliters) of *AzaSite* for the first four years at a per unit price that is specified in the contract. Either party may terminate the agreement upon 60 days' prior written notice if the other party materially breaches the agreement. However, if we fail to make payments to Catalent within 15 days after such payments are due, Catalent may terminate the agreement or Catalent may cease performing under the agreement until all of the outstanding payments are brought current. We may terminate the agreement if a force majeure event prevents Catalent from fully performing its obligations under the agreement for a period of 120 days. In addition, following the conclusion of the third contract year, the agreement may be terminated on 12 months' notice by us or on 24 months' notice by Catalent.

InSite Vision

In February 2007, we entered into a supply agreement with InSite Vision for the active pharmaceutical ingredient, azithromycin. Previously, InSite Vision entered into a third-party supply agreement for the production of azithromycin. Under the supply agreement, InSite Vision agreed to supply our requirements of azithromycin, pursuant to certain forecasting and ordering procedures. The initial term of the supply agreement is until 2012, subject to certain customary termination provisions, such as termination for material breach of the agreement. Either we or InSite Vision may terminate the supply agreement upon 180 days notice to the other party. After 2012, the supply agreement automatically renews for successive three-year periods unless terminated pursuant to such termination provisions. The supply agreement requires that InSite Vision produce for us a specified stockpile of azithromycin.

Yamasa Corporation

Effective September 25, 2009, we entered into a Technology License Agreement for the Manufacture of Denufosol with Yamasa Corporation. During our denufosol development program, Yamasa has manufactured all of the denufosol used by Inspire in its related clinical trials. The purpose of the technology agreement is to facilitate the transfer of the current denufosol manufacturing technology, including intellectual property, to an additional manufacturer and thus enable a two-supplier strategy for denufosol.

Pursuant to the terms and conditions of the technology agreement, Yamasa granted to Inspire an exclusive, worldwide, royalty-free right and license to use, make, have made and sell denufosol and any pharmaceutical formulation containing denufosol as an active pharmaceutical ingredient, under certain intellectual property developed by Yamasa. During the term of the technology agreement, Inspire may designate a single manufacturer (in addition to Yamasa) to use the rights licensed from Yamasa at any given time.

In consideration of the grant of rights under the technology agreement, in October 2009, Inspire paid Yamasa three hundred million Japanese Yen (¥ 300,000,000), which was approximately $3.3 million at the prevailing exchange rate. Additionally, Inspire shall pay Yamasa (i) three hundred million Yen (¥ 300,000,000) within thirty (30) days after the receipt of a process validation report by December 31, 2010 following the successful completion of three validation batches; and (ii) four hundred million Yen (¥ 400,000,000) within thirty (30) days after both (a) the acceptance of a pre-approval inspection of denufosol at Yamasa by the FDA, and (b) the approval of a New Drug Application of a formulated denufosol drug product at Inspire by the FDA.

Patents and Proprietary Rights

We believe that the proprietary protection of our product candidates, processes and know-how is important to the success of our business. We file and prosecute patents covering our proprietary technology and, if warranted, will defend our patents and proprietary technology. We seek trademark protection in the United States and foreign countries, as appropriate. We also rely upon trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain our competitive position.

As of February 28, 2010, our patent estate included approximately 70 U.S. patents that we own or co-own and approximately 20 U.S. patents that we have licensed, as well as over 160 counterpart patents in countries other than the United States. Our issued patents and pending patent applications in the United States include composition of matter coverage on a number of different structural families of compounds as well as related formulation and use coverage. The actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in a particular country.

Below is a summary of certain patent information, as of February 28, 2010, relating to our commercial products as well as product candidates that are in Phase 3 development. The information relating to the products listed below reflects those patents listed in the FDA's Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, with respect to such product. The information relating to *Prolacria* represents those patents listed in our NDA filed with respect to such candidate and the information regarding denufosol tetrasodium reflects the U.S. patents that we own and consider to be particularly important to the protection of such candidate. In addition to the patents reflected in the table, for some of these product candidates we have other patents that cover a particular form or composition or relate to manufacturing methods, as well as pending patent applications. These issued patents and any patents issued in relation to a pending applications, could provide additional or a longer period of protection.

PRODUCTS AND PRODUCT CANDIDATES	NUMBER OF SPECIFIED PATENTS IN U.S.	TYPES OF PATENTS IN U.S.	PATENT OWNER IN U.S.	RANGE OF U.S. PATENT EXPIRATION DATES
Products				
AzaSite	5	Use and Formulation Patents	InSite Vision/ Pfizer[1]	November 2018 – March 2019
Elestat	N/A[2]	N/A[2]	N/A	N/A
Restasis	1	Formulation	Allergan[1]	May 2014
Product Candidates in Phase 3 Clinical Development				
Denufosol tetrasodium	6	Drug substance, Formulation and Use	Inspire	February 2017[3]
Prolacria (diquafosol tetrasodium)	8	Drug substance, Formulation and Use	Inspire	July 2016 – February 2017[3]

(1) In-licensed to Inspire

(2) See "Product—*Elestat*" for a discussion of the expiration of market exclusivity under the Hatch-Waxman Act.

(3) Subject to any applicable patent restoration that may extend protection up to an additional five years from the date of expiration of the applicable patent, if any, for which restoration is sought.

We seek patent protection for our proprietary technology and products in the United States and Canada and in key commercial European and Asia/Pacific countries and other major commercial sectors of the world, as appropriate. We have in-licensed patents related to *AzaSite* in Canada, and have received patents related to denufosol tetrasodium and diquafosol tetrasodium in Canada, Europe, Australia, New Zealand and other Asia/Pacific countries. See "Collaborative Agreements—Allergan, Inc.—*Restasis* and *Prolacria*" and "Collaborative Agreements—Santen Pharmaceutical Co., Ltd." for additional discussion of responsibilities for diquafosol tetrasodium development and potential commercialization outside of the United States.

Competition

Many pharmaceutical and biotechnology companies engage in research and development to commercialize products to treat allergic conjunctivitis, bacterial conjunctivitis, cystic fibrosis, dry eye disease, blepharitis, glaucoma, and other diseases that we are researching. We compete with these companies for funding, access to licenses, personnel, third-party collaborators and product development. However, most large pharmaceutical and biotechnology companies have significantly larger intellectual property estates, substantially greater financial, marketing, sales, distribution and technical resources and greater capabilities and experience in preclinical and clinical development, sales, marketing, manufacturing and regulatory affairs than we do. The introduction of new products or the development of new processes by competitors or new information about existing products may result in price reductions or product replacements, even for products protected by patents.

The following treatments compete, or may compete, with our products and product candidates, as applicable:

Allergic Conjunctivitis. There are multiple therapies available to treat or prevent allergic conjunctivitis. The primary products that *Elestat* competes with are *Patanol*® and *Pataday*™, both by Alcon, Inc.; *Zaditor*® by Novartis and its related generic; and *Optivar*® by Meda Pharmaceuticals and its related generic. *Patanol* and *Pataday* currently have the majority of the prescriptions in the allergic conjunctivitis market. Additionally, in September 2009, the FDA approved *Bepreve™*, by ISTA Pharmaceuticals, Inc., and the product was launched in late 2009.

Bacterial Conjunctivitis. The current prescription ocular anti-infective treatments for bacterial conjunctivitis that compete with *AzaSite* include single-entity antibiotics *Vigamox*® and *Ciloxan*®, both by Alcon; *Zymar*® and *Ocuflox*®, both by Allergan; *Quixin*® and *Iquix*®, both by Vistakon Pharmaceuticals, LLC; and *Besivance*® by Bausch & Lomb, Inc. and combination products such as *Zylet*® by Bausch & Lomb, Inc.; and *TobraDex*® by Alcon. In addition, there are several generics used to treat bacterial conjunctivitis, which include erythromycin, gentamycin and tobramycin.

Cystic Fibrosis. There are two products approved in the United States specifically for the treatment of complications of cystic fibrosis lung disease: *Pulmozyme*®, by Genentech, Inc., an agent designed to break up thickened airway secretions, and *TOBI*®, by Novartis, an inhaled antibiotic. Additionally, in February 2010, the FDA approved *Cayston*® (aztreonam for inhalation), an inhaled antibiotic, by Gilead Sciences, Inc. Academic groups have completed at least one clinical trial that demonstrated clinical benefit of hypertonic saline. At least one clinical trial has been completed that demonstrated clinical benefit with *Zithromax*®, by Pfizer, Inc., an oral antibiotic. In addition, the following products for the treatment of cystic fibrosis are in Phase 3 development: *Bronchitol™* by Pharmaxis and VX-770 by Vertex Pharmaceuticals, Inc.

Dry Eye Disease. The current prescription and non-prescription treatments for dry eye disease include *Restasis* by Allergan; artificial tear solutions and lubricant eye drops. In addition to our development program for *Prolacria*, we are aware of several other companies that are developing products for the treatment of dry eye disease.

Governmental Regulation

The research, development, testing, manufacture, promotion, marketing and distribution of human therapeutic products are extensively regulated by governmental authorities in the United States and other countries. The FDA regulates drugs products in the United States and similar regulatory agencies exist in other countries. The steps ordinarily required before a new drug may be marketed in the United States, which are similar to steps required in most other countries, include:

- Preclinical laboratory tests, preclinical studies in animals and formulation studies and the submission to the FDA of an IND prior to beginning clinical trials for a new drug;
- Adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication;
- The submission of an NDA to the FDA; and
- FDA review and approval of the NDA before any commercial sale or shipment of the drug.

Preclinical tests include laboratory evaluation of product toxicity and formulation, as well as animal studies. The results of preclinical testing are submitted to the FDA as part of an IND. A 30-day waiting period after the filing of each IND is required before the commencement of clinical testing in humans. At any time during this 30-day period or later, the FDA may place a clinical hold and halt proposed or ongoing clinical trials for any one of several conditions that are set out in regulations, and the clinical trial may not resume until the FDA withdraws its hold on the clinical trials. Moreover, positive results of preclinical tests will not necessarily indicate positive results in clinical trials.

Clinical trials to support NDAs are typically conducted in three sequential phases, but the phases may overlap.

Phase 1—During Phase 1, the initial introduction of the drug into healthy volunteers, the drug is tested to assess metabolism, pharmacokinetics and pharmacological actions and safety, including side effects associated with increasing doses.

Phase 2—Phase 2 usually involves studies in a limited patient population to: (1) assess the efficacy of the drug in specific, targeted indications; (2) assess dosage tolerance and optimal dosage; and (3) identify possible adverse effects and safety risks.

Phase 3—If a compound is found to be potentially effective and to have an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials, also called pivotal studies, major studies or advanced clinical trials, are undertaken to further demonstrate clinical efficacy and to further test for safety within an expanded patient population at geographically dispersed clinical trial sites. In general, the FDA requires that at least two adequate and well-controlled Phase 3 clinical trials be conducted.

After successful completion of the required clinical testing, generally an NDA is submitted. The FDA may request additional information before accepting an NDA for filing, in which case the application must be resubmitted with the additional information. Once the submission has been accepted for filing, the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA to an appropriate advisory committee for review, evaluation and recommendation as to scientific issues relevant to whether the application should be approved, but the FDA is not bound by the recommendation of an advisory committee.

Based on its review of the NDA and associated support, such as the results from inspections of manufacturing and clinical sites, the FDA will either approve or refuse to approve the NDA, unless the FDA evaluation is inconclusive, in which case the FDA will issue a "complete response letter." The complete response letter replaced the FDA's "approvable" and "non-approvable" letters on August 11, 2008. A complete response letter will state that the FDA cannot approve the NDA in its present form and, usually, will describe all of the

specific deficiencies that the FDA has identified in the application. The complete response letter, when possible, will include the FDA's recommended actions to place the application in a condition for approval. Deficiencies can be minor (*e.g.*, labeling changes) or major (*e.g.*, requiring additional clinical trials). A complete response letter may also be issued before the FDA conducts the required facility inspection and/or reviews labeling, leaving the possibility that additional deficiencies in the original NDA could be subsequently cited. An applicant receiving a complete response letter is permitted to resubmit the NDA addressing the identified deficiencies (in which case a new two or six month review cycle will begin), or withdraw the NDA. The FDA may consider a failure to take action within one year of a complete response letter to be a request to withdraw, unless the applicant has requested an extension of time in which to resubmit. If the FDA approves an NDA, the marketing of the drug product will be limited to the particular disease states and conditions of use that are described in the product label.

We and all of our contract manufacturers are also required to comply with the applicable FDA cGMP regulations during clinical development and to ensure that the product can be consistently manufactured to meet the specifications submitted in an NDA. The cGMP regulations include requirements relating to product quality as well as the corresponding maintenance of records and documentation. Manufacturing facilities must be approved by the FDA before they can be used to manufacture our products. Based on an inspection, the FDA determines whether manufacturing facilities are in compliance with applicable regulations. Manufacturing facilities in non-U.S. countries that are utilized to manufacture drugs for distribution into the United States are subject to inspection by the FDA. Additionally, failure to comply with local regulatory requirements could affect production and availability of product in relevant markets.

We must also comply with multiple governmental requirements and best practices associated with the marketing, sale and distribution of our products and product samples. These include, but are not limited to, compliance with federal and state reporting laws; review, approval and distribution of product promotional materials; review and monitoring of promotional and educational programs; interactions with health care providers; and distribution of product samples.

With regard to *AzaSite,* we are responsible for monitoring the safety of the product, reporting adverse events, and taking corrective actions as necessary. In addition, we enter into contracts with managed care organizations for both private and government programs, including Medicare Part D and also directly with state and federal governments for certain programs, including Medicaid programs.

Outside the United States, our ability to market our products will also depend on our receipt of marketing authorizations from the appropriate regulatory authorities, as well as the efforts of our collaborative partners to obtain authorizations. The requirements governing the conduct of clinical trials and marketing authorization vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Union procedures are available to companies seeking to market a product in more than one member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, a marketing authorization will be granted. Foreign regulatory approval processes, including those in Europe and Japan, involve risks similar to those associated with obtaining FDA marketing approval.

Health Care Reform Measures and Third-Party Reimbursement

The efforts of governments and third-party payors to contain or reduce the cost of health care will continue to affect the business and financial condition of drug companies. In both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system adopted in recent years that could affect our ability to sell our products profitably, and additional changes could be adopted in the future. For instance, in the United States, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 established a voluntary Medicare outpatient prescription drug benefit under Part D of the Social Security Act. The program, which went into effect January 1, 2006, is administered by the Centers for

Medicare & Medicaid Services, or CMS, within the Department of Health and Human Services, or HHS, and is implemented and operated by private sector Part D plan sponsors. Under the Part D program, each participating drug plan is permitted by regulation to develop and establish its own unique drug formulary that may exclude certain drugs from coverage and impose prior authorization and other coverage restrictions, and negotiate payment levels with drug manufacturers that may be lower than reimbursement levels available through private health plans or other payers. Moreover, beneficiary co-insurance requirements can vary, in turn influencing which products are recommended by physicians and selected by patients. CMS has issued extensive regulations and other subregulatory guidance documents to assist Part D plan sponsors with implementing the new benefit. Moreover, the HHS Office of Inspector General has issued regulations and other guidance in connection with the program. The federal government continues to issue guidance and regulations regarding the obligations of Part D sponsors on an ongoing basis.

Allergan is responsible for the implementation of the Medicare Part D program as it relates to *Restasis* and *Elestat* and has contracted with Part D plan sponsors to cover such drugs under the Part D benefit. We are responsible for contracting with Part D plan sponsors with respect to *AzaSite*. There is no assurance that any drug that we co-promote or sell will be covered by drug plans participating under the Medicare Part D program or, if covered, what the terms of any such coverage will be, or that the drugs will be reimbursed at amounts that reflect current or historical payment levels. Our results of operations could be materially adversely affected by coverage or reimbursement changes resulting from the Medicare prescription drug program, including changes in Part D formularies or prices negotiated with Part D drug plans. To the extent that private insurers or managed care programs follow Medicare coverage and payment developments, the adverse effects of lower Medicare payments may be magnified by private insurers adopting similar lower payment. In addition, health care reform legislation in the United States and in foreign countries, along with other federal or state prescription drug reimbursement and coverage policies, may be enacted or adopted in the future that could further lower payment for our products.

A number of federal and state proposals to reform the health care system have been considered in recent years, and legislation currently is being debated that could impact reimbursement and coverage for prescription drugs. In particular, both the U.S. House of Representatives and Senate approved major health reform plans in late 2009 that would, among many other things: increase Medicaid drug rebate amounts paid by manufacturers and expand the drugs that are subject to such rebates, generally require drug manufacturers to provide a discount on brand-name prescriptions filled in the Medicare Part D "coverage gap," expand comparative effectiveness research programs, and expand disclosure requirements regarding drug manufacturer financial arrangements with referring physicians. In addition, the House version of the bill would establish a public health insurance program to compete with private insurance companies, which could increase competitive pressures in the private insurance market that ultimately could impact prescription drug reimbursement. The House bill also would require the HHS Secretary to negotiate Medicare Part D drug prices directly with pharmaceutical manufacturers, and it would bar agreements between brand name and generic drug manufacturers that delay competition from generic drugs. The Senate bill would impose a $2.3 billion annual fee on the pharmaceutical manufacturing sector, generally allocated according to market share. To date Congress has not reached agreement on a single reform plan, so it is uncertain at this time whether a bill will be enacted in the near future and, if so, the scope of the provisions that will be included or the impact on us. There can be no assurances, however, that enactment of health reform legislation would not have an impact on reimbursement and/or coverage of our products. Likewise, the potential for adoption of health care reform or other cost-control proposals on a state-by-state basis could impact our reimbursement levels and require us to develop state-specific marketing and sales approaches.

Sales of prescription drugs depend significantly on the availability of reimbursement to the consumer and/or provider from third-party payors, such as government health programs and private insurance plans. These third-party payors frequently require that drug companies provide predetermined discounts or rebates from list prices, and they are increasingly challenging the prices for medical products and services. Third-party payors may not consider our products to be cost effective and may not reimburse the consumer sufficiently to allow us, and/or our collaborators, to sell our products on a profitable basis. In addition, an increasing emphasis on managed care

in the United States continues to increase pressure on drug pricing. Additional legislative or regulatory proposals or changes in managed care practices may be adopted that may have an adverse effect on our business and our financial condition, including our profits.

Employees

As of January 31, 2010, we had approximately 240 full-time and part-time employees. In addition, we utilize interns, outside contractors and consultants as needed. Our future success will depend in large part upon our ability to attract and retain highly qualified personnel. Our employees are not represented by any collective bargaining agreements, and we have never experienced a work stoppage. Employees are required to execute confidentiality and assignment of intellectual property agreements.

Available Information

Our Internet site is located at www.inspirepharm.com. Copies of our reports filed pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, including annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports may be accessed from our website, free of charge, as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or SEC. Please note that the information contained on our website is not incorporated by reference into our reports that are filed with the SEC. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street NE, Room 1580, Washington D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is www.sec.gov.

Item 1A. Risk Factors.

RISK FACTORS

An investment in our common stock involves a substantial risk of loss. You should carefully read this entire report and should give particular attention to the following risk factors. You should recognize that other significant risks may arise in the future, which we cannot foresee at this time. Also, the risks that we now foresee might affect us to a greater or different degree than expected. There are a number of important factors that could cause our actual results to differ materially from those indicated by any forward-looking statements in this report. These factors include, without limitation, the risk factors listed below and other factors presented throughout this report and any other reports filed by us with the SEC.

Risks Related to Product Commercialization

Failure to adequately market and commercialize *AzaSite* will negatively impact our revenues.

The commercial success of *AzaSite* will depend on a number of factors, including:

- Acceptance by patients and physicians;
- Effectiveness of our sales and marketing efforts;
- Ability to differentiate *AzaSite* relative to our competitors' products;
- Ability to further develop clinical information to support *AzaSite;*
- Market satisfaction with existing alternative therapies;
- Perceived efficacy relative to other available therapies;
- Disease prevalence;
- Cost of treatment;
- Pricing and availability of alternative products, including generic or over-the-counter products;
- Marketing and sales activities of competitors;
- Shifts in the medical community to new treatment paradigms or standards of care;
- Relative convenience and ease of administration;
- The manufacturer's successful sustaining of manufacturing capability; and
- Our ability to enter into managed care and governmental agreements on favorable terms.

We are responsible for all aspects of the commercialization of this product, including the determination of formularies upon which *AzaSite* is listed, manufacturing, distribution, marketing and sales. The determination of formularies upon which *AzaSite* is listed, the discounts and pricing under such formularies, as well as the amount of time it takes for us to obtain favorable formulary status under various plans will impact our commercialization efforts. Additionally, inclusion on certain formularies requires significant price concessions through rebate programs that impact the level of revenue that we receive. The need to give price concessions can be particularly acute where competing products are listed on the same formulary, such as the area of bacterial conjunctivitis. If *AzaSite* is not successfully commercialized, our revenues will be limited.

Under our agreement with InSite Vision, we are obligated to make pre-determined minimum annual royalty payments to InSite Vision. To the extent annual royalty payments actually paid to InSite Vision on our sales of *AzaSite* are less than the minimum annual royalty amounts established under our agreement with InSite Vision,

we are obligated to pay the difference. In the event we are required to make annual minimum royalty payments, our profits with respect to *AzaSite*, if any, will be decreased or any losses with respect to the product will be increased. Such circumstances may result in us ceasing our commercialization of *AzaSite* and terminating our agreement with InSite Vision.

If *Restasis* is not successfully commercialized by Allergan, our revenues will be negatively impacted.

Allergan is responsible for commercializing *Restasis*. Accordingly, our revenues on the net sales of *Restasis* are dependent on the actions and success of Allergan, over whom we have no control.

Following the expiration of a use patent in August 2009, the manufacture and sale of *Restasis* is protected in the United States by a formulation patent that expires in May 2014. While a formulation patent may afford certain limited protection, a competitor may attempt to gain FDA approval for a cyclosporine product using a different formulation. Furthermore, following the expiration of the formulation patent in 2014, a generic form of *Restasis* could be introduced into the market. If and when *Restasis* experiences competition from a cyclosporine product, including generics, our revenues attributable to *Restasis* may be significantly impacted.

Other factors that could affect the commercialization of *Restasis* include:

- Extent and effectiveness of Allergan's sales and marketing efforts;
- Satisfaction with existing alternative therapies, including generic or over-the-counter products;
- Perceived efficacy relative to other available therapies;
- Changes in, or the levels of, third-party reimbursement of product costs;
- Coverage and reimbursement under Medicare Part D, state government sponsored plans and commercial plans;
- Cost of treatment;
- Development and FDA approval of competing dry eye products; and
- Shifts in the medical community to new treatment paradigms or standards of care.

When a generic form of *Elestat* or an over-the-counter form of epinastine ophthalmic solution is introduced into the market, our agreement with Allergan to co-promote *Elestat* will no longer be in effect, and our revenues from sales of *Elestat* will be minimal.

Our *Elestat* co-promotion agreement with Allergan provides that unless earlier terminated, the term of such agreement will be in effect until the earlier of (i) the approval and launch of the first generic epinastine product after expiration of the FDA exclusivity period covering *Elestat* in the United States, or (ii) the approval and launch of the first over-the-counter epinastine product after expiration of the listing of *Elestat* in the FDA publication Approved Drug Products with Therapeutic Equivalence (commonly called the "Orange Book"). Following the termination of the co-promotion agreement, we will no longer have rights to co-promote *Elestat*. We will be entitled to receive post-termination payments from Allergan, based on any remaining net sales of *Elestat* for a period of 36 months. During the three successive 12-month periods immediately following the termination of the agreement, Allergan will be obligated to pay to us 20%, 15% and 10%, respectively, on any net sales of *Elestat* in the United States.

Subject to applicable law, competitors are permitted to submit to the FDA an ANDA for a generic version of *Elestat*, due to the expiration of the marketing exclusivity period for *Elestat* provided under the Hatch-Waxman Act on October 15, 2008.

We have been notified that Boehringer Ingelheim and Allergan received notices of Paragraph IV certifications from Apotex, Inc., Cypress Pharmaceutical, Inc., Paddock Laboratories, Inc. and Sandoz Inc.

advising that each company filed an ANDA for a generic version of *Elestat*. Each ANDA notice alleges that the method of treatment patent related to *Elestat* is invalid, unenforceable and/or will not be infringed by the respective ANDA applicant's manufacture, use, sale, or offer for sale of the drug for which the ANDA was submitted. The date of submission of the first filing to the FDA Office of Generic Drugs was October 14, 2008, according to the FDA's website (www.fda.gov). In response thereto, Boehringer Ingelheim has filed a statutory disclaimer of all the claims contained in such patent, and accordingly, such patent is unenforceable.

The FDA's review of an ANDA is a confidential process between the FDA and the applicable ANDA filer. We do not expect to be informed by the FDA, any ANDA filer or any other party regarding the status or timing of the review relating to any of the ANDA filings pertaining to a generic form of *Elestat*. The FDA may complete its review of the filed ANDAs at any time. As a result, we expect to be required to stop the co-promotion of *Elestat* with little, if any, advance notice. We believe it is likely that a generic form of epinastine may be launched in the second half of 2010. The loss of co-promotion revenue from *Elestat* will significantly impact our results of operations and cash flows.

If we do not successfully market and promote *Elestat*, our revenues will be negatively impacted.

Notwithstanding the expected termination of the *Elestat* agreement upon the launch of a generic form of *Elestat*, our present revenues depend, in part, upon the continued acceptance of *Elestat* by eye care professionals, allergists and patients. Other factors that could affect the commercialization of *Elestat* include:

- Satisfaction with existing alternative therapies, including therapies requiring only one dose per day;
- Decreases in the size of the market for topical allergic conjunctivitis products;
- Extent and effectiveness of our sales and marketing efforts;
- Changes in, or the levels of, third-party reimbursement of product costs;
- Coverage and reimbursement under Medicare Part D, state government sponsored plans and commercial plans;
- Pricing and availability of alternative products, including generic or over-the-counter products; and
- Marketing and sales activities of competitors.

We rely on third parties to distribute and sell our products and those third parties may not perform.

We are dependent on third parties to perform or assist us in the distribution or sale of *AzaSite,* and are dependent on third parties, primarily Allergan, to perform or assist us in the distribution and sale of *Elestat.* We rely on the services of a single source, third-party distributor to deliver *AzaSite* to our customers. In addition to the physical storage and distribution of *AzaSite,* this third-party distributor maintains and provides us with information and data with regard to our inventory, *AzaSite* orders, billings and receivables, chargebacks and returns, among others, on which our accounting estimates are based. If third parties do not successfully carry out their contractual duties in maximizing the commercial potential of our products, we may be required to hire or expand our own staff and sales force to compete successfully, which may not be possible. If third parties or Allergan do not perform, or assist us in performing these functions, or if there is a delay or interruption in the distribution of our products, it could have an adverse effect on product revenue, accounting estimates and our overall operations.

We depend on three pharmaceutical wholesalers for the vast majority of our *AzaSite* sales in the United States, and the loss of any of these wholesalers would negatively impact our revenues.

The prescription drug wholesaling industry in the United States is highly concentrated, with a vast majority of all sales made by three major full-line companies: Cardinal Health, McKesson Corporation and AmerisourceBergen. Greater than 85% of our *AzaSite* revenues come from sales to these three companies. The loss of any of these wholesalers could have a negative impact on our commercialization of *AzaSite*.

It is also possible that these wholesalers, or others, could decide to change their policies and fees in the future. This could result in or cause us to incur higher product distribution costs, lower margins or the need to find alternative methods of distributing our products. Such alternative methods may not be economically or administratively feasible.

Risks Related to Manufacture and Supply

If we are unable to contract with third parties for the manufacture of active pharmaceutical ingredients required for preclinical testing, for the manufacture of drug products for clinical trials, for the large-scale manufacture of any approved products, or for the manufacture of related devices, we may be unable to develop or commercialize our drug products.

The manufacturing of sufficient quantities of new products or product candidates is a time-consuming and complex process. We have no experience or capabilities to conduct the manufacture of any of our product candidates. In order to successfully commercialize *AzaSite* and continue to develop our product candidates, we need to contract or otherwise arrange for the necessary manufacturing services. There are a limited number of manufacturers that operate under the FDA's cGMP regulations capable of manufacturing for us or our collaborators. We depend upon third parties for the manufacture of active pharmaceutical ingredients, finished drug products for clinical trials, and for the manufacture of *AzaSite*. We expect to depend upon third parties for the large-scale manufacture of commercial quantities of any other approved product. This dependence may adversely affect our ability to develop and deliver such products on a timely and competitive basis. Similarly, our dependence on our partners to arrange for their own supplies of finished drug products may adversely affect our operations and revenues. If we, or our partners, are unable to engage or retain third-party manufacturers on a long-term basis or on commercially acceptable terms, our products may not be commercialized as planned, and the development of our product candidates could be delayed.

Under our agreement with the manufacturer of *AzaSite*, we are required to purchase a minimum number of units of *AzaSite* annually, regardless of our ability to sell *AzaSite*. If we are unable to sell the *AzaSite* that we are required to purchase, our inventory of the product will increase and the shelf life of the inventory will be adversely impacted. In such circumstances, we may be required to make price concessions to sell short-dated product or write-off and dispose of expired product, which may have an adverse affect on our *AzaSite* profitability.

The manufacturing processes for our product candidates have not been validated at the scale required for commercial sales. Delays in scale-up to commercial quantities and any change at the site of manufacture could delay clinical trials, regulatory submissions and ultimately the commercialization of our products. In addition, manufacturing facilities are subject to an FDA inspection to confirm cGMP compliance prior to a product candidate's potential NDA approval as well as ongoing post-approval FDA inspections to ensure continued compliance with cGMP regulations, over which we have no control.

We depend upon a third-party vendor to manufacture the nebulizer used with denufosol with whom we have no supply agreement. This vendor is responsible for managing the manufacturing process of the nebulizer in accordance with all applicable regulatory requirements. Any manufacture or regulatory compliance problems

related to the manufacture of this device or any failure on the part of the manufacturer to supply the device (including discontinuation of the nebulizer) could delay product development or adversely affect regulatory approvals of denufosol.

Reliance on a single party to manufacture and supply either finished product or the bulk active pharmaceutical ingredients for a product or product candidates could adversely affect us.

Under our agreements with Allergan, Allergan is responsible for the manufacture and supply of *Restasis* and *Elestat*. Allergan relies upon an arrangement with a single third party for the manufacture and supply of active pharmaceutical ingredients, or APIs, for each of *Restasis* and *Elestat*. Allergan then completes the manufacturing process to yield finished product.

Under our supply agreement with InSite Vision, InSite Vision is responsible for supplying us with azithromycin, the API used in *AzaSite*. InSite Vision, in turn, relies upon an arrangement with a single third party for the manufacture and supply of such API. We are responsible for producing the finished product form of *AzaSite*, which is currently manufactured by a single party. There can be no assurance that such manufacturer will be able to continue to produce sufficient quantities of finished product in a timely manner to support the commercialization of *AzaSite*.

In the event a third-party manufacturer is unable to supply Allergan or InSite Vision (as the case may be), if such supply is unreasonably delayed, or if Allergan or our finished product contract partner are unable to complete the manufacturing cycle, sales of the applicable product could be adversely impacted, which would result in a reduction in any applicable product revenue. In addition, if Allergan or the third-party manufacturers do not maintain cGMP compliance, the FDA could require corrective actions or take enforcement actions that could affect production and availability of the applicable product, thus adversely affecting sales.

In addition, we rely upon supply agreements with third parties for the manufacture and supply of the bulk APIs for our product candidates for purposes of preclinical testing and clinical trials. We presently depend upon one vendor as the sole manufacturer of our supply of APIs for both *Prolacria* and denufosol. We have entered into an agreement with such manufacturer to facilitate the transfer of the current denufosol manufacturing technology, including intellectual property, to an additional manufacturer and thus enable a two-supplier strategy for denufosol. However, we have not yet entered into an agreement with a secondary supplier for denufosol. Delays in any aspect of implementing the manufacturing process could cause significant development delays and increased costs.

It would be time consuming and costly to identify and qualify new sources for manufacture of APIs or finished products. If our vendors were to terminate our arrangement or fail to meet our supply needs we might be forced to delay our development programs and/or be unable to supply products to the market, which could delay or reduce revenues and result in loss of market share.

The third-party vendor that manufactures denufosol and the API related to both *Prolacria* and Santen's DE-089 does not presently have the capacity to manufacture the projected commercial quantities of API for these products, if any is approved.

Yamasa Corporation manufacturers the clinical supplies of denufosol, and the API (*i.e.* diquafosol) for *Prolacria* and Santen's DE-089. We do not believe that Yamasa presently has the capacity to manufacture the projected commercial quantities of denufosol, or the API for *Prolacria* and Santen's DE-089. Although we have agreements with Yamasa for the manufacture of clinical quantities, we do not have agreements with Yamasa for commercial supplies of denufosol or diquafosol and we are in the process of working to establish those agreements. We may not be able to enter into such agreements on commercially acceptable terms, if at all.

We are in discussions with another manufacturer for the purpose of establishing a secondary source of commercial supply for denufosol. To facilitate this second manufacturer, we entered into an agreement with Yamasa to acquire access to its manufacturing know-how and processes related to denufosol. Technical transfer of manufacturing capabilities, however, can be difficult. Also, we may not be able to enter into secondary supply arrangements on commercially acceptable terms, if at all. A failure to achieve sufficient commercial supply of denufosol could result in a delay in the launch of the candidate. Furthermore, if the candidate is approved, and depending on market acceptance and other competitive factors, a failure to achieve sufficient commercial supply potentially could adversely affect product sales.

In May 2008, Santen filed an application for manufacturing and marketing approval of DE-089 with the Japanese Ministry of Health, Labor, and Welfare, which is pending review. Subject to the terms of our agreement with Santen, we are required to supply Santen with its API requirements for DE-089 for commercial use. We do not have manufacturing expertise, capabilities or facilities, and rely on Yamasa to manufacture this API. We are currently in discussions with Yamasa to further assess its ability to increase capacity for the production of the API for DE-089. If Yamasa is unable to timely produce sufficient commercial quantities of the API for each of DE-089 and *Prolacria*, the launch of each such product candidate following approval, if any, could be delayed. Furthermore, if either DE-089 or *Prolacria* is approved, and depending on market acceptance and other competitive factors, an insufficient supply of the API for such product following its launch potentially could adversely affect product sales. A reduction in sales likely would reduce royalty income to us associated with each of DE-089 and *Prolacria*. If we are unable to supply Santen with its API requirements for DE-089 pursuant to the terms of our agreement, Santen may pursue legal or equitable remedies against us.

Risks Related to Product Development

If the FDA does not conclude that our product candidates meet statutory requirements for safety and efficacy, we will be unable to obtain regulatory approval for marketing in the United States.

We have to conduct significant development activities, non-clinical and clinical tests and obtain regulatory approval before our product candidates can be commercialized. Product candidates that may appear to be promising at early stages of development may not successfully reach the market for a number of reasons. The results of preclinical and clinical testing of our product candidates under development may not necessarily indicate the results that will be obtained from later or more extensive testing. Additionally, companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. Our ongoing clinical trials might be delayed or halted for various reasons, including:

- The measure of efficacy of the drug is not statistically significant compared to placebo;
- Patients experience severe side effects or serious adverse events during treatment;
- Patients die during the clinical trial because their disease is too advanced or because they experience medical problems that may or may not relate to the drug being studied;
- Patients do not enroll in the clinical trials at the rate we expect;
- We decide to modify the drug or the clinical trial protocol during testing;
- Our commercial partners, or future commercial partners, delay, amend or change our development plan or strategy; and
- We allocate our limited financial and other resources to other clinical and preclinical programs.

Changes in regulatory policy or new regulations as well as clinical investigator misconduct could also result in delays or rejection of our applications for approval of our product candidates. Clinical investigator misconduct that raises questions about the integrity of data in one or more applications (e.g., fraud, bribery, omission of a

material fact, gross negligence) could be used by the FDA as grounds to suspend substantive scientific review of all pending marketing applications until the data in question have successfully undergone a validity assessment. Product candidates that fail validity assessments must be withdrawn from FDA review or, if the drug is an approved, marketed product, such product must be removed from the market.

Additionally, the introduction of our products in foreign markets will subject us to foreign regulatory clearances, the receipt of which may be unpredictable, uncertain and may impose substantial additional costs and burdens which we or our partners in such foreign markets may be unwilling or unable to fund. As with the FDA, foreign regulatory authorities must be satisfied that adequate evidence of safety and efficacy of the product has been presented before marketing authorization is granted. The foreign regulatory approval process includes all of the risks associated with obtaining FDA marketing approval. Approval by the FDA does not ensure approval by other regulatory authorities, nor does approval by any foreign regulatory authority ensure approval by the FDA.

Since some of our clinical candidates utilize new or different mechanisms of action and in some cases there may be no regulatory precedents, conducting clinical trials and obtaining regulatory approval may be difficult, expensive and prolonged, which would delay any commercialization of our products.

To complete successful clinical trials, our product candidates must demonstrate safety and provide substantial evidence of efficacy. The FDA generally evaluates efficacy based on the statistical significance of a product candidate meeting predetermined clinical endpoints. The design of clinical trials to establish meaningful endpoints is done in collaboration with the FDA prior to the commencement of clinical trials. We establish these endpoints based on guidance from the FDA, including FDA guidance documents applicable to establishing the efficacy, safety and tolerability measures required for approval of products. However, since some of our product candidates utilize new or different mechanisms of action, the FDA may not have established guidelines for the design of our clinical trials and may take longer than average to consider our product candidates for approval. The FDA could change its view on clinical trial design and establishment of appropriate standards for efficacy, safety and tolerability and require a change in clinical trial design, additional data or even further clinical trials before granting approval of our product candidates. We could encounter delays and increased expenses in our clinical trials if the FDA concludes that the endpoints established for a clinical trial do not adequately predict a clinical benefit.

We are developing denufosol as an inhaled product candidate for the treatment of cystic fibrosis. Denufosol tetrasodium is a first-in-class ion channel regulator that addresses the underlying ion transport defect in the lungs of patients with cystic fibrosis. The FDA has not published guidance on the drug approval process associated with such a product candidate. Furthermore, we are not aware of any FDA-approved product that addresses the underlying ion transport defect in the lungs of patients with cystic fibrosis. We cannot predict or guarantee the outcome or timing of our Phase 3 program for denufosol for cystic fibrosis. A significant amount of work will be required to advance denufosol through clinical testing, including satisfactory completion of additional clinical trials and other studies. We may later decide to change the focus or timing of our Phase 3 program. Our TIGER-2 clinical trial for denufosol for cystic fibrosis may not be successful or unexpected safety concerns may emerge that would negatively change the risk/benefit profile for this product candidate.

We have initiated a Phase 2 development program to evaluate the use of *AzaSite* for the treatment of blepharitis. The FDA has not published guidelines on the approval of a product for the treatment of blepharitis. Furthermore, to date, no prescription product has been approved by the FDA for the treatment of blepharitis. The FDA may require that we evaluate the product in relation to different primary and/or secondary clinical endpoints than those being used presently. This may require us to undertake additional Phase 2 clinical trials, which could lead to increased costs and program delays.

The FDA has not published guidelines on the approval of a product for the treatment of dry eye disease. In order to gain approval, it will be necessary to undertake at least one additional Phase 3 clinical trial in support of our NDA for *Prolacria.* There can be no guarantee that any such additional clinical trial would be successful or that the FDA would approve *Prolacria* even if such additional clinical trial was successful.

We may need to develop alternate dosing regimens for our product candidates.

In order to achieve broad market acceptance of our product candidates, we may need to develop, alone or with others, alternate dosing regimens and methods for administering our products. For example, in our current clinical trials, denufosol for the treatment of cystic fibrosis is administered by a standard nebulizer three times per day, but clinical data from our TIGER-1 clinical trial indicated that patients in that study administered the drug only 2.7 times per day, on average. Patients may prefer a smaller, more portable device or less frequent dose administration. In addition, we intend that *Prolacria* will be applied from a vial containing a single day's dosage of non-preserved medication. Patients may prefer to purchase preserved medication for multiple doses. Neither we nor Allergan have established a plan to develop a multi-dose formulation.

Similar challenges may exist in identifying and developing appropriate and convenient dosing and methods of administration for our other product candidates. If the number of doses, or the method of dosing, is not convenient, patients may not use our product. Furthermore, if patients use our products at a dosing level that is less than the dosing level tested in our clinical trials, the drug may not be efficacious or may be less efficacious. In such cases, the patient may look for alternative therapies.

Estimated development costs are difficult to project and may change frequently prior to regulatory approval.

The number and type of studies that may be required by the FDA, or other regulatory authorities, for a particular compound are based on the compound's clinical profile compared to existing therapies for the targeted patient population. While all new compounds require standard regulated phases of testing, the actual type and scope of testing can vary significantly among different product candidates and as a result, creates additional complexity when estimating program costs. Factors that affect the costs of a clinical trial include:

- The number of patients required to participate in clinical trials to demonstrate statistical significance for a drug's safety and efficacy and the number and geographical location of clinical trial sites necessary to enroll such patients;
- The time required to enroll the targeted number of patients in clinical trials, which may vary depending on the size and availability of the targeted patient population and the perceived benefit to the clinical trial participants; and
- The number and type of required laboratory tests supporting clinical trials.

Additionally, ongoing development programs and associated costs are subject to frequent, significant and unpredictable changes due to a number of factors, including:

- Data collected in preclinical or clinical trials may prompt significant changes, delays or enhancements to an ongoing development program;
- Commercial partners and the underlying contractual agreements may require additional or more involved clinical or preclinical activities;
- The FDA or other regulatory authorities may direct the sponsor to change or enhance its ongoing development program based on developments in the testing of similar compounds or related compounds;
- Unexpected regulatory requirements, changes in regulatory policy or review standards, or interim reviews by regulatory agencies may cause delays or changes to development programs; and

- Anticipated manufacturing costs may change significantly due to necessary changes in manufacturing processes, variances from anticipated manufacturing process yields or changes in the cost and/or availability of starting materials, and other costs to ensure the manufacturing facility is in compliance with cGMP requirements and is capable of consistently producing the product candidate in accordance with established specifications submitted to the FDA.

The occurrence of any of these factors may result in significant disparities in total costs required to complete the respective development programs.

Clinical trials may take longer to complete and cost more than we expect, which would adversely affect our ability to commercialize product candidates and achieve profitability.

Clinical trials are expensive and are often lengthy. They require appropriate identification of optimal treatment regimens and relevant patient population, adequate supplies of drug product, and sufficient patient enrollment. Patient enrollment is a function of many factors, including:

- The size and availability of the relevant patient population;
- The nature of the protocol;
- The proximity of patients to clinical sites;
- The eligibility criteria for the clinical trial; and
- The perceived benefit of participating in a clinical trial.

Delays in patient enrollment can result in increased costs and longer development times. Even if we successfully complete clinical trials, we may not receive regulatory approval for the product candidate. In addition, if the FDA or foreign regulatory authorities require additional clinical trials, we could face increased costs and significant development delays.

We are conducting portions of our TIGER-2 clinical trial in Canada, Australia and New Zealand and are therefore subject to the risks and uncertainties of doing business internationally. Disruptions in communication and transportation, changes in governmental policies, and currency exchange rates, among other factors, may affect the time and costs required to complete these clinical trials.

If we fail to reach milestones or to make annual minimum payments or otherwise breach our obligations under our license agreements, our licensors may terminate our agreements with them.

If we fail to meet payment obligations, performance milestones relating to the timing of regulatory filings, development and commercial diligence obligations, fail to make milestone payments in accordance with applicable provisions, or fail to pay the minimum annual payments under our respective licenses, our licensors may terminate the applicable license. As a result, our development of the respective product candidate or commercialization of the product would cease.

Risks Related to Governmental Regulation

Failure to comply with all applicable regulations, including those that require us to obtain and maintain governmental approvals for our product candidates, may result in fines, corrective actions, administrative sanctions and restrictions, including the withdrawal of a product from the market.

Pharmaceutical companies are subject to significant regulation by a number of local, state, and federal governmental agencies, including the FDA. Such regulations and their authorizing statutes are amended from time to time. There are laws and regulations that govern areas including financial controls, clinical trials, testing, manufacturing, labeling, safety, packaging, shipping, distribution, post-approval safety surveillance, marketing, and promotion of pharmaceuticals, including those governing interactions with prescribers and health care

professionals in a position to prescribe, recommend, or arrange for the provision of our products. Failure to comply with applicable regulatory requirements could, among other things, result in warning letters, fines, corrective actions, administrative sanctions, suspensions or delays of product manufacture or distribution or both, product recalls, delays in marketing activities and sales, withdrawal of marketing approvals, and civil or criminal sanctions including seizure of product, court-ordered injunction, and possible exclusion from eligibility for federal government contracts payment of our products by Medicare, Medicaid, and other third-party payors.

After initial regulatory approval, the manufacturing and marketing of drugs, including our products, are subject to continuing FDA and foreign regulatory review. The FDA requires drug manufacturers and distributors to monitor the safety of a drug after it is approved and marketed. We are required to document and investigate reports of adverse events and report serious adverse events to the FDA. Additionally, the FDA encourages health professionals to report significant adverse events associated with products. The FDA may require additional clinical studies, known as Phase 4 studies, to evaluate product safety effects. In addition to studies required by the FDA after approval, we may conduct our own Phase 4 studies to explore the use of the approved drug product for treatment of new indications or to broaden our knowledge of the product. The subsequent discovery of previously unknown problems with a product's safety or efficacy as a result of these studies or as reported in their prescribed use may result in restrictions through labeling changes or withdrawal of the product from the market.

The FDA periodically inspects drug manufacturing facilities to ensure compliance with applicable cGMP regulations. Failure to comply with statutory and regulatory requirements subjects the manufacturer to possible legal or regulatory action, such as suspension of manufacturing, seizure of product or court-ordered injunction, which could include mandatory recall of a product. Before taking such actions, the FDA may first issue one or more notices of compliance deficiencies. Such notices include inspectional observations on Form FDA-483, warning letters, and other untitled written correspondence; however, the FDA may also take action without such notice in situations of egregious noncompliance or where public safety is at risk. The FDA may also request us to take actions voluntarily or we may initiate actions ourselves such as recalls or suspension of manufacturing to ensure compliance with cGMP regulations.

Additional authority to take post-approval actions was given to the FDA under the FDA Amendments Act of 2007. The FDA is authorized to revisit and change its prior determinations if new information raises questions about our product's safety profile. The FDA is authorized to impose additional post-marketing requirements which could result in actions such as requiring additional studies, corrective actions, fines, withdrawal of marketing approval, or any combination of such actions.

In its regulation of advertising, the FDA may issue correspondence to pharmaceutical companies alleging that its advertising, promotional materials or activities are false or misleading. Pharmaceutical advertising and promotional activity must be true, fairly balanced between benefits and risks, provide adequate risk information, and be within the labeled indications. Drug manufacturers are prohibited from promoting a product for any use that is not on the approved labeling; however, healthcare professionals are free to use the product for any use that, in the judgment of the healthcare professional, may be appropriate for any individual patient. The FDA has the power to impose a wide array of sanctions on companies for advertising practices that it concludes is false or misleading, and, if we were to receive correspondence from the FDA alleging such practices, it may be necessary for us to:

- Incur substantial expenses, including fines, penalties, legal fees and costs to conform to the FDA's limits on such promotion;
- Change our methods of marketing, promoting and selling products;
- Take corrective action, which could include placing advertisements or sending letters to physicians correcting statements made in previous advertisements or promotions; or
- Disrupt the distribution of products and stop sales until we are in compliance with the FDA's interpretation of applicable laws and regulations.

Medicare prescription drug coverage legislation and future legislative or regulatory reform of the health care system may affect our or our partners' ability to sell products profitably.

In both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could affect our ability to sell our products profitably. In the United States, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 established a voluntary Medicare outpatient prescription drug benefit under Part D of the Social Security Act. The program, which went into effect January 1, 2006, is administered by the Centers for Medicare & Medicaid Services within the Department of Health and Human Services and is implemented and operated by private sector Part D plan sponsors. Each participating drug plan is permitted by regulation to develop and establish its own unique drug formulary that may exclude certain drugs from coverage and impose prior authorization and other coverage restrictions, and negotiate payment levels with drug manufacturers that may be lower than reimbursement levels available through private health plans or other payers. Moreover, beneficiary co-insurance requirements can vary, which could influence which products are recommended by physicians and selected by patients. The federal government can be expected to continue to issue guidance and regulations regarding the obligations of Part D sponsors under the program.

Allergan is responsible for the implementation of the Medicare Part D program as it relates to *Restasis* and *Elestat* and has contracted with Part D plan sponsors to cover such drugs under the Part D benefit. We are responsible for contracting with Part D plan sponsors with respect to *AzaSite*. There is no assurance that any drug that we co-promote or sell will be covered by drug plans participating under the Medicare Part D program or, if covered, what the terms of any such coverage will be, or that the drugs will be reimbursed at amounts that reflect current or historical payment levels. Our results of operations could be materially adversely affected by the reimbursement changes emerging from Medicare prescription drug coverage legislation or from changes in the formularies or price negotiations with Part D drug plans. To the extent that private insurers or managed care programs follow Medicare coverage and payment developments, the adverse effects of lower Medicare payment may be magnified by private insurers adopting similar lower payment.

Our products also can be impacted by state and federal legislative and regulatory changes in Medicaid reimbursement policy and in mandated levels of Medicaid drug rebates paid by pharmaceutical manufacturers. Congress is considering proposals as part of health reform that would increase the drug rebate level paid by pharmaceutical manufacturers to Medicaid for brand-name drugs and make other changes that could result in larger pharmaceutical manufacturer rebate obligations. Likewise, many states are facing serious budgetary pressures that could lead to adoption of cost-containment measures, including provisions aimed at reducing Medicaid drug prices. There can be no assurances that new federal or state policies will not increase our rebate obligation or lower Medicaid reimbursement levels for our products.

New federal or state drug payment changes or health care reforms in the United States and in foreign countries may be enacted or adopted in the future that could further lower payment for our products. In particular, both the U.S. House of Representatives and Senate approved major health reform plans in late 2009. In addition to increasing Medicaid drug rebate obligations, the legislation generally would require drug manufacturers to provide a discount on brand-name prescriptions filled in the Medicare Part D "coverage gap"; expand comparative effectiveness research programs, and expand disclosure requirements regarding drug manufacturer financial arrangements with referring physicians. The House version of the bill also would establish a public health insurance program to compete with private insurance companies, which could increase competitive pressures in the private insurance market that ultimately could impact prescription drug reimbursement. The House bill also would require the HHS Secretary to negotiate Medicare Part D drug prices directly with pharmaceutical manufacturers, and it would bar agreements between brand name and generic drug manufacturers that delay competition from generic drugs. The Senate bill would impose a $2.3 billion annual fee on the pharmaceutical manufacturing sector, generally allocated according to market share. To date Congress has not reached agreement on a single reform plan, so it is uncertain at this time whether a bill will be enacted in the near future and, if so, the scope of the provisions that will be included or the impact on us. There can be no

assurances, that enactment of health reform legislation would not have an adverse impact on reimbursement and/or coverage of our products. Likewise, the potential for adoption of health care reform or other cost-control proposals on a state-by-state basis could impact our reimbursement levels and require us to develop state-specific marketing and sales approaches.

Congress also has enacted the American Recovery and Reinvestment Act, which included a major expansion of federal efforts to compare the effectiveness of different medical treatments, including pharmaceuticals, which eventually could impact Medicare and private payer coverage and payment policies. The federal government may consider additional proposals that could lead to reimbursement constraints and restrictions on access to certain products. We cannot predict the outcome of such initiatives, and it is difficult to predict the impact on our business of future legislative and regulatory changes.

We are subject to "fraud and abuse" and similar government laws and regulations, and a failure to comply with such laws and regulations, or an investigation into our compliance with such laws and regulations, or a failure to prevail in any litigation related to noncompliance, could harm our business.

We are subject to multiple state and federal laws pertaining to health care fraud and abuse. Pharmaceutical pricing, sales, and marketing programs and arrangements, and related business practices in the health care industry generally are under increasing scrutiny from federal and state regulatory, investigative, prosecutorial, and administrative entities. Many health care laws, including the federal and state anti-kickback laws and federal and state statutory and common law false claims laws, have been construed broadly by the courts and permit government entities to exercise considerable discretion. In the event that any of these government entities believed that wrongdoing had occurred, one or more of them could institute civil, administrative, or criminal proceedings which, if instituted and resolved unfavorably, could subject us to substantial fines, penalties, and injunctive and administrative remedies, including exclusion from government reimbursement programs. We cannot predict whether investigations or enforcement actions would affect our marketing or sales practices. Any such result could have a material adverse impact on our results of operations, cash flows, financial condition, and our business. Such investigations and enforcement actions could be costly, divert management's attention from our business, and result in damage to our reputation. We cannot guarantee that measures that we have taken to prevent violations, including our corporate compliance program, will protect us from future violations, lawsuits or investigations by governmental entities or private whistleblowers. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant negative impact on our business, including the imposition of significant fines or other sanctions.

Congress also is considering new and expanded federal fraud authorities as part of health reform legislative efforts. We cannot predict at this time whether health reform legislation will be enacted and, if so, the extent of new fraud authorities that would be adopted, if any, or the potential impact on our business.

Failure to adequately ensure compliance with applicable laws and regulations may subject us to whistleblower and government actions.

In recent years, pharmaceutical companies have been the targets of extensive whistleblower actions in which the person bringing the action alleges violations of the federal civil False Claims Act or its state equivalent, including allegations that manufacturers aided and abetted in the submission of false claims. These actions have focused on such areas as pricing practices, off-label product promotion, sales and marketing practices, and improper relationships with physicians and other health care professionals, among others. If our relationships with health care professionals and/or our promotional or other activities fail to comply with applicable laws, regulations or guidelines, we may be subject to warnings from, or enforcement action by, regulatory and other federal or state governmental authorities. The potential ramifications are far-reaching if there are areas identified as out of compliance by regulatory agencies and governmental authorities including, but not limited to, significant financial penalties, manufacturing and clinical trial consent decrees, commercialization restrictions, exclusion from government programs, product recalls or seizures, the imposition of corporate integrity

agreements and deferred prosecution agreements, or other restrictions and litigation. Furthermore, there can be no assurance that we will not be subject to a whistleblower or other state or federal investigative or enforcement action at some time in the future. Even an unsuccessful challenge to our operations or activities could prove costly and divert management's attention.

Risks Associated with Our Business and Industry

If we do not receive timely regulatory approvals of our product candidates and successfully launch such products, we may need substantial additional funds to support our expanding capital requirements.

We have used substantial amounts of cash to fund our research and development and commercial activities. Our operating expenses were approximately $129.8 million and $120.2 million for the years ended December 31, 2009 and 2008, respectively. Our cash, cash equivalents and investments totaled approximately $129.1 million on December 31, 2009. Based on current operating plans, we expect our cash and investments to provide liquidity beyond 2010.

We expect that our capital and operating expenditures will continue to exceed our revenue over the next several years as we conduct our research and development and commercial activities. Many factors will influence our future capital requirements, including:

- The number, breadth and progress of our research and development programs;
- The level of activities relating to commercialization of our products;
- The ability to attract collaborators for our products and establish and maintain those relationships;
- Achievement of milestones under our existing or future collaborations and licensing agreements;
- Progress by our collaborators with respect to the development of product candidates;
- Competing technological and market developments;
- The timing and terms of any business development activities;
- The timing and amount of debt repayment requirements;
- The costs involved in defending any litigation claims against us;
- The costs involved in responding to government, the Financial Industry Regulatory Authority, Inc., or other applicable investigations against us; and
- The costs involved in enforcing patent claims and other intellectual property rights.

In addition, our capital requirements will depend upon:

- The level of sales generated for *AzaSite, Restasis* and *Elestat*;
- The receipt of revenue from Allergan on net sales of *Restasis* and *Elestat*;
- The receipt of revenue from wholesalers and other customers on net sales of *AzaSite;*
- The receipt or payment of milestone payments under our current collaborative agreements and any future collaborations;
- The ability to obtain approval from the FDA for our product candidates; and
- Payments from existing and future collaborators.

In the event that we do not receive timely regulatory approvals, we may need substantial additional funds to fully develop, manufacture, market and sell all of our other potential products and support our on-going product

commercialization and co-promotion efforts. We may seek such additional funding through public or private equity offerings and debt financings. Additional financing may not be available when needed. If available, such financing may not be on terms favorable to us or our stockholders. Our stockholders' ownership will be diluted if we raise additional capital by issuing equity securities. If we are required to raise funds through future collaborations and licensing arrangements, we may have to give up rights to our technologies or product candidates or grant licenses on unfavorable terms. If adequate funds are not available, we would have to scale back or terminate research programs and product development and we may not be able to successfully commercialize any product candidate.

Our co-promotion and royalty revenues are based, in part, upon Allergan's revenue recognition policy and other accounting policies over which we have limited or no control.

We recognize co-promotion revenue based on Allergan's net sales of *Elestat* and royalty revenue based on Allergan's net sales of *Restasis,* as defined in the co-promotion agreements and as reported to us by Allergan. Accordingly, our co-promotion and royalty revenues are based upon Allergan's revenue recognition policy and other accounting policies over which we have limited or no control and the underlying terms of our co-promotion agreements. Allergan's filings with the SEC indicate that Allergan maintains disclosure controls and procedures in accordance with applicable laws, which are designed to provide reasonable assurance that the information required to be reported by Allergan in its Exchange Act filings is reported timely and in accordance with applicable laws, rules and regulations. We are not entitled to review Allergan's disclosure controls and procedures. All of our co-promotion and royalty revenues are currently derived from Allergan's net sales of *Restasis* and *Elestat* as reported to us by Allergan. We are unable to provide complete assurance that Allergan will not revise reported revenue amounts in the future. If Allergan's reported revenue amounts were inaccurate, it could have a material impact on our financial statements, including financial statements for previous periods.

Revenues in future periods could vary significantly and may not cover our operating expenses.

Our revenues may fluctuate from period to period due in part to:

- The timing of the introduction of a generic form of *Elestat*;
- Fluctuations in future sales of *AzaSite, Restasis* and *Elestat* due to competition, the intensity of an allergy season, disease prevalence, manufacturing difficulties, reimbursement and pricing under commercial or government plans, seasonality, or other factors that affect the sales of a product;
- Deductions from gross sales relating to estimates of sales returns, credits and allowances, normal trade and cash discounts, managed care sales rebates and other allocated costs;
- The duration of market exclusivity of *AzaSite* and *Restasis*;
- The timing of approvals, if any, for other possible future products;
- The progress toward and the achievement of developmental milestones by us or our partners;
- The initiation of new contractual arrangements with other companies; and
- The failure or refusal of a collaborative partner to pay royalties or milestone payments.

Inventory levels of *AzaSite* held by wholesalers can also cause our operating results to fluctuate unexpectedly. Although we attempt to monitor wholesaler inventory of our products, we rely upon information provided by third parties to quantify the inventory levels maintained by wholesalers. In addition, we and the wholesalers may not be effective in matching inventory levels to end-user demand. Significant differences between actual and estimated inventory levels and product demand may result in inadequate or excessive (1) inventory production, (2) product supply in distribution channels, (3) product availability at the retail level, and (4) unexpected increases or decreases in orders from our major customers. Any of these events may cause our revenues to fluctuate significantly from quarter to quarter, and in some cases may cause our operating results for a particular quarter to be below expectations.

If we are unable to make the scheduled principal and interest payments on our term loan facility or maintain minimum liquidity levels or compliance with other debt covenants as defined in the loan and security agreement, we may default on our debt.

Our $60.0 million term loan facility is collateralized by substantially all of our assets, except for our intellectual property, but including all accounts, license and royalty fees and other revenues and proceeds arising from our intellectual property. Under the agreement, we are required to maintain minimum liquidity levels based on the balance of the outstanding advances. The agreement also includes a subjective acceleration clause that provides our lenders with the ability to accelerate repayment, even if we are in compliance with all conditions of the agreement, upon a material adverse change to our business, properties, assets, financial condition or results of operations. The agreement may affect our operations in several ways, including the following:

- A portion of our cash flow from operations will be dedicated to the payment of the principal and interest on our indebtedness;
- Our future cash flow may be insufficient to meet our required principal and interest payments;
- We may need to raise additional capital in order to remain in compliance with the loan covenants;
- Our ability to enter into certain transactions (including incurrences of indebtedness) may be limited; and
- We may need to delay or reduce planned expenditures for clinical trials as well as other development and commercial activities if our current operations are not sufficient enough to service our debt.

Events of default under the loan and security agreement are not limited to, but include the following:

- Payment default;
- Covenant default;
- A material adverse change in our business operations;
- Breach of our agreements with Allergan; and
- Judgments against us over a specified dollar amount.

In case of an uncured default, the following actions may be taken against us by the lending institutions:

- All outstanding obligations associated with the term loan facility would be immediately due and payable;
- Any of our balances and deposits held by the lending institutions would be applied to the obligation;
- Balances and accounts at other financial institutions could be "held" or exclusive control could be transferred to the lending institutions; and
- All collateral, as defined in the agreement, could be seized and disposed of.

If we continue to incur operating losses for a period longer than anticipated, or in an amount greater than anticipated, we may be unable to continue our operations.

We have experienced significant losses since inception. We incurred net operating losses of approximately $40.0 million and $51.6 million for the years ended December 31, 2009 and 2008, respectively. As of December 31, 2009, our accumulated deficit was approximately $400.4 million. We currently expect to incur operating losses over the next several years. We expect that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial. Such fluctuations will be affected by the timing and level of the following:

- Commercialization activities to support *AzaSite* and *Elestat*;
- Revenues from *Restasis*;
- Regulatory approvals of our product candidates;

- Patient demand for our products and any licensed products;
- Payments to and from licensors and corporate partners;
- Research and development activities;
- Investments in new technologies and product candidates; and
- The costs involved in defending any litigation claims against, or government investigations of, us.

To achieve and sustain profitable operations, we must, alone or with others, develop successfully, obtain regulatory approval for, manufacture, introduce, market and sell our products. The time frame necessary to achieve market success is long and uncertain. We may not generate sufficient product revenues to become profitable or to sustain profitability. If the time required to achieve profitability is longer than we anticipate, we may not be able to continue our operations.

The current stock market and credit market conditions are extremely volatile and unpredictable. It is difficult to predict whether these conditions will continue or worsen, and, if so, whether the conditions would impact us and whether such impact could be material.

We have exposure to many different industries and counterparties, including commercial banks, investment banks and customers (which include wholesalers, managed care organizations and governments) that may be unstable or may become unstable in the current economic environment. Any such instability may impact these parties' ability to fulfill contractual obligations to us or they might limit or place burdensome conditions upon future transactions with us. Customers may also reduce spending during times of economic uncertainty. Also, it is possible that suppliers may be negatively impacted. If such events were to occur, there could be a resulting material and adverse impact on our operations and results of operations.

We may decide to access the equity or debt markets to meet capital or liquidity needs. However, the constriction and volatility in these markets may restrict our future flexibility to do so when such needs arise. Further, recent economic conditions have resulted in severe downward pressure on the stock and credit markets, which could reduce the return available on invested corporate cash, which if severe and sustained could have a material and adverse impact on our results of operations and cash flows.

Our dependence on collaborative relationships may lead to delays in product development, lost revenues and disputes over rights to technology.

Our business strategy depends to some extent upon the formation of research collaborations, licensing and/or marketing arrangements. We currently have collaboration agreements with several collaborators, including Allergan, InSite Vision and Santen. The termination of any collaboration will result in the loss of any unmet development or commercial milestone payments, may lead to delays in product development and disputes over technology rights, and may reduce our ability to enter into collaborations with other potential partners. In the event we breach an agreement with a collaborator, the collaborator is entitled to terminate our agreement with them in the event we do not cure the breach within a specified period of time, which is typically 60 or 90 days from the notice date. With respect to the Allergan collaboration, in the event we become an affiliate of a third party that manufactures, markets or sells any then currently promoted prescription ophthalmic product, Allergan will have the right to terminate our *Elestat* co-promotion agreement, which right must be exercised within 3 months of the occurrence of such event. If we do not maintain our current collaborations, or establish additional research and development collaborations or licensing arrangements, it will be difficult to develop and commercialize potential products. Any future collaborations or licensing arrangements may not be on terms favorable to us.

Our current or any future collaborations or licensing arrangements ultimately may not be successful. Under our current strategy, and for the foreseeable future, we do not expect to develop or market products outside North

America without a collaborative partner or outside our therapeutic areas of focus. We are currently pursuing the out-licensing of certain rights related to our cystic fibrosis program. We may be unsuccessful in out-licensing this program or we may be forced to out-license this program on terms that are not favorable to us.

It may be necessary in the future for us to obtain additional licenses to avoid infringement of third-party patents. Additionally, we may enter into license arrangements with other third parties as we build our product portfolio. We do not know the terms on which such licenses may be available, if at all.

We will continue to depend on collaborators and contractors for the preclinical study and clinical development of therapeutic products and for manufacturing and marketing of potential products. Our agreements with collaborators typically allow them some discretion in electing whether to pursue such activities. If any collaborator were to breach or terminate its agreement with us or otherwise fail to conduct collaborative activities in a timely and successful manner, the clinical development or commercialization of product candidates or research programs would be delayed or terminated. Any delay or termination in clinical development or commercialization would delay or eliminate potential product revenues relating to our product candidates.

Disputes may arise in the future over the ownership of rights to any technology developed with collaborators. These and other possible disagreements between us and our collaborators could lead to delays in the collaborative development or commercialization of products. Such disagreements could also result in litigation or require arbitration to resolve.

Failure to hire and retain key personnel may hinder our product development programs and our business efforts.

We depend on the principal members of management and scientific staff, including Adrian Adams, our President and Chief Executive Officer and a director, and Thomas R. Staab, II, our Chief Financial Officer and Treasurer. If these people leave us, we may have difficulty conducting our operations. Other than Mr. Adams, with whom we have an employment agreement, we have not entered into agreements with any other officers or any other members of our management and scientific staff that bind them to a specific period of employment. Our future success will depend in part on our ability to attract, hire or appoint, and retain additional personnel skilled or experienced in the pharmaceutical industry. There is significant competition for such qualified personnel and we may not be able to attract and retain such personnel.

We may not be able to successfully compete with other biotechnology companies and established pharmaceutical companies.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. There are many companies seeking to develop products for the same indications that we are working on. Our competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical and chemical companies and specialized biotechnology firms.

Most of these competitors have greater resources than we do, including greater financial resources, larger research and development staffs and more experienced marketing and manufacturing organizations. In addition, most of our competitors have greater experience than we do in conducting clinical trials and obtaining FDA and other regulatory approvals. Accordingly, our competitors may succeed in obtaining FDA or other regulatory approvals for product candidates more rapidly than we do. Companies that complete clinical trials, obtain required regulatory approvals, and commence commercial sale of their drugs before we do may achieve a significant competitive advantage, including patent and FDA marketing exclusivity rights that would delay our ability to market products. Drugs resulting from our research and development efforts, or from our joint efforts with our collaborative partners, may not compete successfully with competitors' existing products or products under development.

Our competitors may also develop technologies and drugs that are safer, more effective, or less costly than any we are developing or which would render our technology and future drugs obsolete and non-competitive. In addition, alternative approaches, such as gene therapy, in treating diseases that we have targeted, such as cystic fibrosis, may make our product candidates obsolete.

If our intellectual property protection is inadequate, the development and any possible sales of our product candidates could suffer or competitors could force our products completely out of the market.

Our business and competitive position depends on our ability to continue to develop and protect our products and processes, proprietary methods and technology and to prevent others from infringing on our patents, trademarks and other intellectual property rights. Upon the expiration or loss of patent protection for a product, we or our applicable collaborative partners may lose a significant portion of sales of that product in a short period of time as other companies manufacture generic forms of the previously protected product or manufacture similar products at lower cost, without having had to incur significant research and development costs in formulating the product. Therefore, our future financial success may depend in part on our and our partners obtaining patent protection for technologies incorporated into our products. We cannot assure that such patents will be issued, or that any existing or future patents will be of commercial benefit. In addition, it is impossible to anticipate the breadth or degree of protection that any such patents will afford, and we cannot assure that any such patents will not be successfully challenged in the future. If we are unsuccessful in obtaining or preserving patent protection, or if any of our products rely on unpatented proprietary technology, we cannot assure that others will not commercialize products substantially identical to those products. We also believe that the protection of our trademarks is an important factor in product recognition and in our ability to maintain or increase market share. If we do not adequately protect our rights in our various trademarks from infringement, their value to us could be lost or diminished, seriously impairing our competitive position. Moreover, the laws of certain foreign countries do not protect our intellectual property rights to the same extent as the laws of the United States.

Certain of our patents are use patents containing claims covering methods of treating disorders and diseases by administering therapeutic chemical compounds. Use patents may provide limited protection for commercial efforts in the United States, but may afford a lesser degree of protection, if any, in other countries due to their patent laws. Besides our use patents, we have patents and patent applications covering compositions (new chemical compounds), pharmaceutical formulations and processes for manufacturing our new chemical compounds. Many of the chemical compounds included in the claims of our use patents and process applications were known in the scientific community prior to our patent applications. None of our composition patents or patent applications covers these previously known chemical compounds, which are in the public domain. As a result, competitors may be able to commercialize products that use the same previously known chemical compounds used by us for the treatment of disorders and diseases not covered by our use patents. Such competitors' activities may reduce our revenues.

Third parties may challenge, invalidate or circumvent our patents and patent applications relating to our products, product candidates or technologies at any time. If we must defend a patent suit, or if we choose to initiate a suit to have a third-party patent declared invalid, we may need to make considerable expenditures of money and management time in litigation. We believe that there is significant litigation in the pharmaceutical and biotechnology industry regarding patent and other intellectual property rights. A patent does not provide the patent holder with freedom to operate in a way that infringes the patent rights of others. We may be accused of patent infringement at any time. A judgment against us in a patent infringement action could cause us to pay monetary damages, require us to obtain licenses, or prevent us from manufacturing or marketing the affected products. In addition, we may need to initiate litigation to enforce our proprietary rights against others. Initiation of litigation may result in considerable expenditures of money and management time and may result in our patents being declared invalid. Further, we may need to participate in interference proceedings in the U.S. Patent and Trademark Office, or USPTO, to determine the priority of invention of any of our technologies.

Our ability to develop sufficient patent rights in our pharmaceutical, biopharmaceutical and biotechnology products to support commercialization efforts is uncertain and involves complex legal and factual questions. For instance, the USPTO examiners may not allow our claims in examining our patent applications. If we have to appeal a decision to the USPTO's Appeals Board for a final determination of patentability, we could incur significant legal fees. Lengthy and uncertain patent prosecutions, including the utilization of the appeals process, can add uncertainty, delay and expense to the process of obtaining intellectual property rights for our products, and as such may add delay and uncertainty to the development program for any such product.

Use of our products may result in product liability claims for which we may not have adequate insurance coverage.

Manufacturing, marketing and sale of our products or conducting clinical trials of our product candidates may expose us to liability claims from the use of those products and product candidates. Product liability claims could result in the imposition of substantial liability on us, a recall of products, or a change in the indications for which they may be used. Although we carry product liability insurance and clinical trial liability insurance, we, or our collaborators, may not maintain sufficient insurance to cover these potential claims. We do not have the financial resources to self-insure and it is unlikely that we will have these financial resources in the foreseeable future. If we are unable to protect against potential product liability claims adequately, we may find it difficult or impossible to continue to commercialize our products or the product candidates we develop. If claims or losses exceed our liability insurance coverage, we may go out of business.

Insurance coverage is increasingly more costly and difficult to obtain or maintain.

While we currently have insurance for our business, property, directors and officers, and our products, insurance is increasingly more costly and narrower in scope, and we may be required to assume more risk in the future. If we are subject to claims or suffer a loss or damage in excess of our insurance coverage, we will be required to share that risk in excess of our insurance limits. If we are subject to claims or suffer a loss or damage that is outside of our insurance coverage, we may incur significant uninsured costs associated with loss or damage that could have an adverse effect on our operations and financial position. Furthermore, any claims made on our insurance policies may impact our ability to obtain or maintain insurance coverage at reasonable costs or at all.

Risks Related to Our Stock

Our common stock price has been volatile and your investment in our stock may decline in value.

The market price of our common stock has been volatile. These fluctuations create a greater risk of capital losses for our stockholders as compared to less volatile stocks. Factors that have caused volatility and could cause additional volatility in the market price of our common stock include among others:

- Announcements made by us concerning results of clinical trials with our product candidates;
- Announcements regarding the commercialization of *AzaSite*;
- Announcements regarding FDA approval of *Prolacria*, denufosol or any of our product candidates;
- Market acceptance and market share of *AzaSite, Restasis* and *Elestat*;
- The timing of the introduction of a generic form of *Elestat;*
- Duration of market exclusivity of *AzaSite* and *Restasis*;
- Volatility in other securities including pharmaceutical and biotechnology securities;
- Changes in government regulations;

- Regulatory actions and/or investigations;
- Changes in the development priorities of our collaborators that result in changes to, or termination of, our agreements with such collaborators;
- Developments concerning proprietary rights including patents by us or our competitors;
- Variations in our operating results;
- FDA approval of other treatments for the same indication as any one of our product candidates;
- Business development activities; and
- Litigation.

Extreme price and volume fluctuations occur in the stock market from time to time that can particularly affect the prices of biotechnology companies. These extreme fluctuations are sometimes unrelated to the actual performance of the affected companies.

Warburg is able to exercise substantial control over our business.

Warburg Pincus Private Equity IX, L.P., or Warburg, holds 22,907,488 shares of our common stock, which represented approximately 28% of our outstanding common stock as of January 31, 2010. Warburg and its affiliates may acquire the lesser of: (x) 32.5% of our voting securities on a fully diluted basis and (y) 34.9% of our then outstanding voting securities, without triggering the provisions of our stockholder rights plan. Warburg has the right to designate one person for election to our Board of Directors for so long as Warburg owns a significant percentage of our securities. Pursuant to this right, Jonathan S. Leff serves as a Class C member of the Board of Directors. Pursuant to a Securities Purchase Agreement, dated July 17, 2007, for so long as Warburg owns at least 10% of the shares of common stock issued upon the exchange of Exchangeable Preferred Stock it acquired in July 2007, it will have subscription rights to acquire a pro rata amount of future issuances of equity securities by us, subject to certain exceptions. As a result of the foregoing, Warburg is able to exercise substantial influence over our business, policies and practices.

Our existing principal stockholders hold a substantial amount of our common stock and may be able to influence significant corporate decisions, which may conflict with the interest of other stockholders.

As of January 31, 2010, our current 5% and greater stockholders (which includes Warburg) and their affiliates beneficially owned approximately 42% of our outstanding common stock. These stockholders, if they act together, may be able to influence the outcome of matters requiring approval of the stockholders, including the election of our directors and other corporate actions such as:

- a merger or corporate combination with or into another company;
- a sale of substantially all of our assets; and
- amendments to our certificate of incorporation.

The decisions of these individual stockholders may conflict with our interests or those of our other stockholders.

Future sales and issuances of securities may dilute the ownership interests of our current stockholders and cause our stock price to decline.

Future sales of our common stock by current stockholders into the public market could cause the market price of our stock to fall. As of January 31, 2010, there were 82,350,770 shares of our common stock outstanding. In addition, after deducting the $115 million of common stock sold in August 2009, we retain the

ability to issue and may in the future issue, up to an additional $15 million of securities, including common stock, preferred stock, debt securities, depositary shares and securities warrants, from time to time at prices and on terms to be determined at the time of sale remaining under an active shelf registration statement, which we filed with the SEC on March 9, 2007. Furthermore, we may from time to time issue securities in relation to a license arrangement, collaboration, merger or acquisition.

Up to 16,178,571 shares of our common stock are issuable upon the release of restricted stock units and/or exercise of stock options that have been, or stock options, stock appreciation rights, stock awards and restricted stock units that may be, issued pursuant to our Amended and Restated 1995 Stock Plan, our Amended and Restated 2005 Equity Compensation Plan and the Executive Employment Agreement, dated February 18, 2010, between Inspire and Mr. Adams. The shares underlying existing stock options and restricted stock units and possible future stock options, stock appreciation rights and stock awards have been registered pursuant to registration statements on Form S-8.

If some or all of such shares are sold or otherwise issue into the public market over a short period of time, our current stockholders' ownership interests may be diluted and the value of all publicly traded shares is likely to decline, as the market may not be able to absorb those shares at then-current market prices. Additionally, such sales and issuances may make it more difficult for us to sell equity securities or equity-related securities in the future at a time and price that our management deems acceptable, or at all.

Our Rights Agreement, the provisions of our Change in Control Severance Benefit Plans, the anti-takeover provisions in our Amended and Restated Certificate of Incorporation, as amended, and Amended and Restated Bylaws, standstill agreements, and our right to issue preferred stock, may discourage a third party from making a take-over offer that could be beneficial to us and our stockholders and may make it difficult for stockholders to replace our Board of Directors and effect a change in our management if they desire to do so.

In October 2002, we entered into a Rights Agreement with Computershare Trust Company. The Rights Agreement could discourage, delay or prevent a person or group from acquiring 15% or more of our common stock. The Rights Agreement provides that if a person acquires 15% or more of our common stock without the approval of our Board of Directors, all other stockholders will have the right to purchase securities from us at a price that is less than its fair market value, which would substantially reduce the value of our common stock owned by the acquiring person. As a result, our Board of Directors has significant discretion to approve or disapprove a person's efforts to acquire 15% or more of our common stock. In connection with the transaction with Warburg, we and Computershare entered into a First Amendment to Rights Agreement which provides that Warburg and its affiliates will be exempt from the definition of an "Acquiring Person" under the Rights Agreement, unless Warburg or certain of its affiliates becomes the beneficial owner of the lesser of: (x) 32.5% of our voting securities on a fully diluted basis and (y) 34.9% of our then outstanding voting securities. In addition to Warburg's ability to exercise substantial control over our business, the First Amendment to Rights Agreement could further discourage, delay or prevent a person or group from acquiring 15% or more of our common stock. As part of the same transaction with Warburg, we entered into a standstill agreement, dated July 20, 2007, pursuant to which Warburg and certain of its affiliates agreed for three years not to increase their holdings of our common stock beyond the levels described above in the First Amendment to Rights Agreement. On August 4, 2009, we amended the standstill agreement to extend its term until August 4, 2012.

Our employees are covered under Change in Control Severance Benefit Plans which provide severance benefits in the event of a change of control that occurs prior to July 8, 2010, and in the event they are terminated after a change in control occurring on or after July 8, 2010. In addition, Mr. Adam's Executive Employment Agreement provides for severance benefits in the event of a change of control. These arrangements would increase the acquisition costs to a purchasing company that triggers the change in control provisions and as a result, may discourage, delay or prevent a change in control.

Our Amended and Restated Certificate of Incorporation, as amended, and Amended and Restated Bylaws contain provisions which could discourage, delay or prevent a third party from acquiring shares of our common stock or replacing members of our Board of Directors. Our Amended and Restated Certificate of Incorporation, as amended, allows our Board of Directors to issue shares of preferred stock. Our Board of Directors can determine the price, rights, preferences and privileges of those shares without any further vote or action by the stockholders. As a result, our Board of Directors could make it difficult for a third party to acquire a majority of our outstanding voting stock. Since management is appointed by the Board of Directors, any inability to effect a change in the Board of Directors may result in the entrenchment of management.

Our Amended and Restated Certificate of Incorporation, as amended, also provides that the members of the Board will be divided into three classes. Each year, the terms of approximately one-third of the directors will expire. Our Amended and Restated Bylaws include director nomination procedures and do not permit our stockholders to call a special meeting of stockholders. The staggering of directors' terms of office, the director nomination procedures and the inability of stockholders to call a special meeting may make it difficult for stockholders to remove or replace the Board of Directors should they desire to do so. The director nomination requirements include a provision that requires stockholders give advance notice to our Secretary of any nominations for director or other business to be brought by stockholders at any stockholders' meeting. Our directors may be removed from our Board of Directors only for cause. These provisions may discourage, delay or prevent changes of control or management, either by third parties or by stockholders seeking to change control or management.

In the ordinary course of our business, from time to time we discuss possible collaborations, licenses and other transactions with various third parties, including pharmaceutical companies and biotechnology companies. When we deem it appropriate, we enter into standstill agreements with such third parties in relation to the discussions. These standstill agreements, several of which are currently in force, typically prohibit such parties from acquiring our securities for a period of time.

We are also subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. Under these provisions, if anyone becomes an "interested stockholder," we may not enter a "business combination" with that person for three years without special approval, which could discourage a third party from making a take-over offer and could delay or prevent a change of control. For purposes of Section 203, "interested stockholder" means, generally, someone owning 15% or more of our outstanding voting stock or an affiliate of ours that owned 15% or more of our outstanding voting stock during the past three years, subject to certain exceptions as described in Section 203. In connection with our prior sale of stock to Warburg, we agreed to waive Warburg's acquisition of securities from the provisions of Section 203 of the Delaware General Corporation Law.

FORWARD LOOKING STATEMENTS

This annual report on Form 10-K, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, that are subject to the "safe harbor" created by those sections. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as "anticipate," "estimate," "plan," "project," "continuing," "believe," "expect," "future" and "intend" and similar expressions to identify forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated by any forward-looking statements, including, without limitation, the risk factors listed above and those relating to product development, revenue and earnings expectations, intellectual property rights and litigation, competitive products, results of clinical trials, the need for additional research and testing,

delays in manufacturing, funding and the timing and content of decisions made by regulatory authorities, including the FDA and other factors presented throughout this annual report and any other documents filed by us with the SEC.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this annual report on Form 10-K or in any document incorporated by reference might not occur. Stockholders are cautioned not to place undue reliance on the forward-looking statements, which speak only of the date of this report or the date of the document incorporated by reference in this document. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

Item 1B. Unresolved Staff Comments

On December 10, 2009, we received a comment letter from the staff of the SEC with respect to our Form 10-K for the fiscal year ended December 31, 2008 and our Proxy Statement filed March 26, 2009. We responded to the SEC's comments on February 1, 2010, and received two follow-up comments from the SEC on March 11, 2010, regarding a tabular summary of various patent information and asking for confirmation that the Compensation Discussion and Analysis to be contained in our upcoming proxy statement will discuss the factors considered by our Compensation Committee in evaluating the portion of the bonuses to our named executive officers that were based on individual contributions. On March 12, 2010, we submitted a response to the SEC that we believe addresses their comments. However, this has not been confirmed by the SEC.

Item 2. Properties.

We lease contiguous administrative and laboratory facilities that comprise approximately 51,000 square feet in Durham, North Carolina, which is adjacent to the Research Triangle Park. The various leases underlying our facilities expire in January 2011 and are renewable. We believe our facilities are adequate to meet our current operational needs. In addition, we lease approximately 500 square feet of administrative space as a sales office in Dallas, Texas.

Item 3. Legal Proceedings.

Not applicable.

Item 4. Reserved.

PART II

Item 5. Market for the Company's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Our common stock has been traded on the Nasdaq National Market, and later the Nasdaq Global Market, under the symbol "ISPH" since August 3, 2000. The following table sets forth, for the calendar periods indicated, the range of high and low sale prices for our common stock on the Nasdaq Global Market:

2008	High	Low
First Quarter	$6.09	$3.59
Second Quarter	$6.75	$2.89
Third Quarter	$4.70	$3.21
Fourth Quarter	$4.08	$1.68

2009	High	Low
First Quarter	$4.21	$2.59
Second Quarter	$5.70	$3.52
Third Quarter	$6.54	$4.33
Fourth Quarter	$6.07	$4.36

As of January 31, 2010, there were 50 record stockholders and approximately 5,600 beneficial stockholders of our common stock. As of January 29, 2010, the last sale price reported on the Nasdaq Global Market for our common stock was $5.51 per share.

We have not paid or declared dividends on our common stock since our inception and do not plan to pay dividends on our common stock in the foreseeable future. Any earnings that we may realize will be retained to finance our growth.

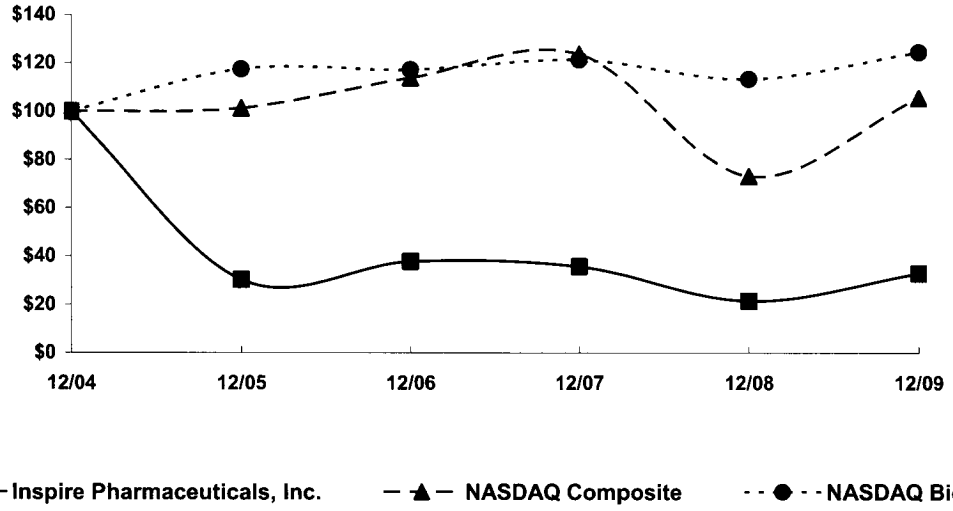
See "Part III—Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" for certain equity compensation plan information.

RELATIVE STOCK PERFORMANCE

The graph below compares Inspire Pharmaceuticals, Inc.'s cumulative 5-year total stockholder return on common stock with the cumulative total returns of the NASDAQ Composite index and the NASDAQ Biotechnology index. The graph tracks the performance of a $100 investment in our common stock and in each of the indexes (with the reinvestment of all dividends) from December 31, 2004 to December 31, 2009.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among Inspire Pharmaceuticals, Inc., The NASDAQ Composite Index
And The NASDAQ Biotechnology Index



*$100 invested on 12/31/04 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

	Cumulative Total Returns					
	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08	12/31/09
Inspire Pharmaceuticals, Inc.	**$100.00**	**$ 30.29**	**$ 37.87**	**$ 35.66**	**$ 21.47**	**$ 32.92**
NASDAQ Composite	**100.00**	**101.33**	**114.01**	**123.71**	**73.11**	**105.61**
NASDAQ Biotechnology	**100.00**	**117.54**	**117.37**	**121.37**	**113.41**	**124.58**

The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock.

Item 6. Selected Financial Data.

The selected statement of operations data and balance sheet data with respect to the years ended December 31, 2009, 2008, 2007, 2006 and 2005 set forth below are derived from our financial statements. The selected financial data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in Item 7 below, and our financial statements and the notes thereto appended to this annual report. Historical results are not necessarily indicative of our future results.

	(in thousands, except per share amounts)				
	Year Ended December 31,				
	2009	2008	2007	2006	2005
Statement of Operations Data:					
Revenue	$ 92,159	$ 70,498	$ 48,665	$ 37,059	$ 23,266
Operating expenses:					
Cost of sales	11,271	6,412	1,622	—	—
Research and development	51,134	44,637	53,391	42,537	23,566
Selling and marketing	49,304	54,568	45,543	25,265	23,223
General and administrative	16,053	14,540	13,986	15,880	12,004
Restructuring	2,014	—	—	—	—
Total operating expenses	129,776	120,157	114,542	83,682	58,793
Loss from operations	(37,617)	(49,659)	(65,877)	(46,623)	(35,527)
Other income/(expense), net	(2,359)	(1,944)	2,137	4,508	3,680
Net loss	$(39,976)	$(51,603)	$(63,740)	$(42,115)	$(31,847)
Non-cash deemed dividend related to beneficial conversion feature of exchangeable preferred stock	—	—	(8,285)	—	—
Net loss attributable to common stockholders	$(39,976)	$(51,603)	$(72,025)	$(42,115)	$(31,847)
Net loss per common share—basic and diluted	$ (0.60)	$ (0.91)	$ (1.61)	$ (1.00)	$ (0.76)
Common shares used in computing weighted average common shares outstanding—basic and diluted	66,797	56,609	44,763	42,227	42,101

	(in thousands)				
	December, 31				
	2009	2008	2007	2006	2005
Balance Sheet Data:					
Cash, cash equivalents and investments	$129,099	$ 72,966	$139,724	$102,281	$122,323
Trade receivables, net	22,682	16,544	12,974	8,245	4,898
Inventories, net	1,717	689	1,280	—	—
Working capital	85,412	52,512	107,651	89,655	99,265
Total assets	178,770	114,224	180,503	116,699	132,446
Deferred revenue	—	—	371	—	—
Debt obligations, including current portion[1]	25,175	43,605	57,701	21,357	1,392
Total stockholders' equity	119,168	44,387	91,693	78,371	118,689
Shares of common stock outstanding	82,346	56,672	56,501	42,238	42,211

(1) Includes capital leases.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Cautionary Statement

The discussion below contains forward-looking statements regarding our financial condition and our results of operations that are based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted within the United States, as well as projections for the future. The preparation of these financial statements requires our management to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. We evaluate our estimates on an ongoing basis. Our estimates are based on historical experience and on various other assumptions that are believed to be reasonable under the circumstances. The results of our estimates form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources.

We operate in a highly competitive environment that involves a number of risks, some of which are beyond our control. We are subject to risks common to biopharmaceutical companies, including risks inherent in our research, development and commercialization efforts, clinical trials, uncertainty of regulatory actions and marketing approvals, reliance on collaborative partners, enforcement of patent and proprietary rights, the need for future capital, competition associated with products, potential competition associated with our product candidates and retention of key employees. In order for any of our product candidates to be commercialized, it will be necessary for us, or our collaborative partners, to conduct clinical trials, demonstrate efficacy and safety of the product candidate to the satisfaction of regulatory authorities, obtain marketing approval, enter into manufacturing, distribution and marketing arrangements, obtain market acceptance and adequate reimbursement from government and private insurers. We cannot provide assurance that we will generate significant revenues or achieve and sustain profitability in the future. In addition, we can provide no assurance that we will have sufficient funding to meet our future capital requirements. Statements contained in Management's Discussion and Analysis of Financial Condition and Results of Operations which are not historical facts are, or may constitute, forward-looking statements. Forward-looking statements involve known and unknown risks that could cause our actual results to differ materially from expected results. The most significant known risks are discussed in the section entitled "Risk Factors." Although we believe the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

Our revenues are difficult to predict and depend on numerous factors. The effectiveness of our ability and the ability of third parties on which we rely to help us manufacture, distribute and market *AzaSite;* physician and patient acceptance of *AzaSite;* competitor response to *AzaSite;* as well as discounts, pricing and coverage on governmental and commercial formularies; are all factors, among others, that will impact the level of revenue recorded for *AzaSite* in subsequent periods. Through the year ended December 31, 2008, we actively promoted both *Restasis* and *Elestat* through our commercial organization. As of January 1, 2009, we are no longer responsible for the co-promotion of *Restasis*, but we continue to receive royalties on Allergan's net sales of *Restasis*. Our co-promotion and royalty revenues are based upon Allergan's revenue recognition policy and other accounting policies, over which we have limited or no control, and on the underlying terms of our co-promotion agreements. Our co-promotion and royalty revenues are impacted by the number of governmental and commercial formularies upon which *Restasis* and *Elestat* are listed, the discounts and pricing under such formularies, as well as the estimated and actual amount of rebates, all of which are managed by Allergan. Other factors that are difficult to predict and that impact our co-promotion and royalty revenues are the extent and effectiveness of Allergan's sales and marketing efforts, our sales and marketing efforts, coverage and reimbursement under Medicare Part D and Medicaid programs, and the sales and marketing activities of competitors. Additionally, our ability to receive revenues on future sales of *AzaSite*, *Restasis* and *Elestat* are dependent upon the duration of market exclusivity and strength of patent protection. Revenues related to development activities are dependent upon the progress toward and the achievement of developmental milestones by us or our collaborative partners.

Our operating expenses are also difficult to predict and depend on several factors. Cost of sales related to *AzaSite* contain variable and fixed cost components. Research and development expenses, including expenses for development milestones, drug manufacturing, and clinical research activities, depend on the ongoing requirements of our development programs, completion of business development transactions, availability of capital and direction from regulatory agencies, which are difficult to predict. Management may in some cases be able to control the timing of research and development expenses, in part by accelerating or decelerating clinical development activities, but many of these expenditures will occur irrespective of whether our product candidates are approved when anticipated or at all. We have incurred and expect to continue to incur significant selling and marketing expenses to commercialize our products. Again, management may in some cases be able to control the timing and magnitude of these expenses.

As a result of these factors, we believe that period to period comparisons are not necessarily meaningful and you should not rely on them as an indication of future performance. Due to all of the foregoing factors, it is possible that our operating results will be below the expectations of market analysts and investors. In such event, the prevailing market price of our common stock could be materially adversely affected.

Overview

We are a biopharmaceutical company focused on researching, developing and commercializing prescription pharmaceutical products for ophthalmic and pulmonary diseases. Our goal is to build and commercialize a sustainable portfolio of innovative new products based on our technical and scientific expertise. The most advanced compounds in our clinical pipeline are denufosol tetrasodium for cystic fibrosis and *Prolacria* for dry eye, both of which are in Phase 3 development, and *AzaSite* for blepharitis, which is in Phase 2 development. We receive revenue related to the promotion of *AzaSite* for bacterial conjunctivitis, co-promotion of *Elestat* for allergic conjunctivitis and royalties on *Restasis* for dry eye.

In February 2007, we signed an exclusive licensing agreement with InSite Vision for the U.S. and Canadian commercialization rights of *AzaSite* for the treatment of bacterial conjunctivitis. In April 2007, *AzaSite* was approved by the FDA for the treatment of bacterial conjunctivitis in adults and children one year of age and older. In August 2007, we launched *AzaSite* in the United States and are promoting it to eye care specialists.

In 2004, we launched *Elestat* for the treatment of allergic conjunctivitis and began co-promoting *Restasis* for the treatment of dry eye disease. In December 2008, we amended our agreement with Allergan and terminated our co-promotion responsibilities related to *Restasis*. Under agreements with Allergan, we receive revenue based upon Allergan's net sales of these products.

See Part I—Item 1. Business of this report for a full discussion of our agreements with InSite Vision, Allergan and other significant collaborative agreements, as well our other product candidates in clinical development.

We have incurred significant operating losses since our inception and, as of December 31, 2009, we had an accumulated deficit of $400.4 million. Revenue from sales of *AzaSite, Restasis* and *Elestat* did not exceed our total operating expenses in 2009. We expect to incur operating losses for the next several years. We have financed our operations through the sale of equity securities, including private sales of preferred stock and public offerings of common stock, debt, and with revenue from corporate partnerships, including co-promotion and royalty revenue. We operate as a single business segment and do not have any foreign operations.

Critical Accounting Policies and Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our financial statements and the related disclosures, which have been prepared in accordance with generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and

judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosure of contingent assets and liabilities. We evaluate our estimates, judgments and the policies underlying these estimates on a periodic basis, as situations change and regularly discuss financial events, policies, and issues with members of our audit committee and our independent registered public accounting firm. In addition, recognition of revenue from product co-promotion and earned royalties is affected by certain estimates and judgments made by Allergan on which we rely when recording this revenue. We routinely evaluate our estimates and policies regarding revenue recognition, product returns, rebates and incentives, inventory and manufacturing, taxes, stock-based compensation, research and development, marketing and other expenses and any associated liabilities.

We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates and judgments about matters that are inherently uncertain.

Revenue Recognition

We record all of our revenue from: (1) sales of *AzaSite*; (2) product co-promotion activities and earned royalties; and (3) collaborative research agreements when realized or realizable and earned. Revenue is realized or realizable and earned when all of the following criteria are met: 1) persuasive evidence of an arrangement exists; 2) delivery has occurred or services have been rendered; 3) the seller's price to the buyer is fixed or determinable; and 4) collectibility is reasonably assured.

Product Revenues

We recognize revenue for sales of *AzaSite* when title and substantially all the risks and rewards of ownership have transferred to the customer, which generally occurs on the date of shipment, with the exception of transactions whereby product stocking incentives were offered approximately one month prior to the product's August 13, 2007 launch. In the United States, we sell *AzaSite* to wholesalers and distributors, who, in turn, sell to pharmacies and federal, state and commercial health care organizations.

Sales deductions consist of statutory rebates to state Medicaid, Medicare and other government agencies, contractual rebates with commercial managed care organizations, wholesaler chargebacks, sales discounts (including trade discounts and distribution service fees), allowances for coupon and voucher programs and product returns. These deductions are recorded as reductions to revenue from *AzaSite* in the same period as the related sales with estimates of future utilization derived from historical experience adjusted to reflect known changes in the factors that impact such reserves.

We utilize data from external sources to help us estimate our gross-to-net sales adjustments as they relate to the recognition of revenue for *AzaSite* sold. External sourced data includes, but is not limited to, information obtained from certain wholesalers with respect to their inventory levels and sell-through to customers, targeted surveys as well as data from IMS Health, a third-party supplier of market research data to the pharmaceutical industry. We also utilize this data to help estimate and identify prescription trends and patient demand, as well as product levels in the supply chain.

We account for these sales deductions in accordance with the Financial Accounting Standards Board, or FASB, authoritative guidance on revenue recognition when consideration is given by a vendor to a customer as well as when the right of return exists.

We have categorized and described more fully, the following significant sales deductions, all of which involve estimates and judgments which we consider to be critical accounting estimates, and require us to use information from external sources.

Rebates and Chargebacks

Statutory rebates to state Medicaid agencies and Medicare and contractual rebates to commercial managed care organizations are based on statutory or negotiated discounts to the selling price. As it can take up to nine months or more for information to be received on actual usage of *AzaSite* in managed care and Medicaid and other governmental programs as well as on the total discounts to be reimbursed, we maintain reserves for amounts payable under these programs relating to *AzaSite* sales.

Chargebacks claimed by wholesalers are based on the differentials between product acquisition prices paid by wholesalers and lower government contract pricing paid by eligible customers covered under federally qualified programs.

The amount of the reserve for rebates and chargebacks is based on multiple qualitative and quantitative factors, including the historical and projected utilization levels, historical payment experience, changes in statutory laws and interpretations as well as contractual terms, product pricing (both normal selling prices and statutory or negotiated prices), changes in prescription demand patterns and utilization of our product through private or public benefit plans, and the levels of *AzaSite* inventory in both the wholesale and retail distribution channel. Other factors that we may consider, if determined relevant would include price changes from competitors and introductions of generics and/or competitive new products. We acquire prescription utilization data from IMS Health, a third-party supplier of market research data to the pharmaceutical industry. We apply these multiple factors, the quantitative historical data along with other qualitative aspects, such as management's judgment regarding future utilization trends, to the respective period's sales of *AzaSite* to determine the rebate accrual and related expense. We update our estimates and assumptions each period and record any necessary adjustments to our reserves. Settlements of rebates and chargebacks typically occur within nine months from point of sale. To the extent actual rebates and chargebacks differ from our estimates, additional reserves may be required or reserves may need to be reversed, either of which would impact current period product revenue. As of December 31, 2009 and 2008, reserves for rebates and chargebacks were $3.5 million and $783,000, respectively.

Discounts and Other Sales Incentives

Discounts and other sales incentives consist of the following:

- *Prompt pay discounts*—Prompt payment discounts are offered to all wholesalers in return for payment within 30 days following the invoice date. We record sales of *AzaSite* net of the discount amount based on historical experience. We adjust the reserve at the end of each reporting period to approximate the percentage discount applicable to the outstanding gross accounts receivable balances.
- *Inventory Management Agreement ("IMA") Fees*—Per contractual agreements with our largest wholesalers (which collectively represented over 85% of 2009 *AzaSite* sales), we provide an IMA fee based on a percentage of their purchases of *AzaSite*. The IMA fee rates are set forth in the individual contracts. We track sales to these wholesalers each period and accrue a liability relating to the unpaid portion of these fees by applying the contractual rates to such sales.
- *Product coupons and vouchers*—Product coupons and vouchers offer patients the ability to receive free or discounted product through their pharmacy or prescribing physician, to whom we provide an inventory of coupons or vouchers as applicable. We use a third-party administrator who invoices us on a periodic basis for the cost of coupons and vouchers redeemed in the period. We base our estimates on the historical coupon and voucher redemption rate of similar programs.

As of December 31, 2009 and 2008, reserves for discounts and other sales incentives were $889,000 and $519,000, respectively.

Product Returns

At the time of sale of *AzaSite*, we record product returns allowances based on our estimate of the portion of sales that will be returned by our customers in the future. The return allowances are established in accordance with our return policy. Our return goods policy generally allows for returns of *AzaSite* within an 18-month period, from six months prior to the expiration date and up to 12 months following the expiration date, but may differ from customer to customer, depending on certain factors. Future estimated returns of *AzaSite* are based primarily on the return data for comparative products and our own historical experience with *AzaSite*. Historical returns data on *AzaSite* is analyzed on a specific production lot basis. In determining our return allowance we also consider other relevant factors, including:

- Levels of inventory in the distribution channel and any significant changes to these levels
- Estimated expiration date or remaining shelf life of inventory in the distribution channel
- Current and projected demand of *AzaSite* that could be impacted by introductions of generic products and/or introductions of competitive new products; and
- Competitive product recalls and/or discontinuances

Our estimates of the level of *AzaSite* inventory in the distribution channel is based on inventory data provided by wholesalers; and third-party prescription data. As of December 31, 2009 and 2008, reserves for returns of *AzaSite* were $1.5 million and $701,000, respectively.

The following table reflects the gross to net sales accruals and the balance in the related allowance accounts for the years ended December 31, 2009, 2008 and 2007.

	Balance at Beginning of Year	Related to Current Period Sales	Related to Prior Period Sales	Credits/ Payments	Balance at End of Year
Year Ended December 31, 2009					
Reserve for Rebates and Chargebacks	$ 783,000	$ 6,015,000	$188,000	$(3,498,000)	$3,488,000
Reserve for Discounts and Other Sales Incentives	519,000	3,328,000		(2,958,000)	889,000
Allowance for Returns	701,000	1,259,000	301,000	(738,000)	1,523,000
Total Sales Deductions Accruals	$2,003,000	$10,602,000	$489,000	$(7,194,000)	$5,900,000
Year Ended December 31, 2008					
Reserve for Rebates and Chargebacks	$ 149,000	$ 1,501,000	$ (7,000)	$ (860,000)	$ 783,000
Reserve for Discounts and Other Sales Incentives	89,000	1,394,000		(964,000)	519,000
Allowance for Returns	95,000	661,000	16,000	(71,000)	701,000
Total Sales Deductions Accruals	$ 333,000	$ 3,556,000	$ 9,000	$(1,895,000)	$2,003,000
Year Ended December 31, 2007					
Reserve for Rebates and Chargebacks	$ —	$ 154,000	$ —	$ (5,000)	$ 149,000
Reserve for Discounts and Other Sales Incentives		270,000		(181,000)	89,000
Allowance for Returns		118,000		(23,000)	95,000
Total Sales Deductions Accruals	$ —	$ 542,000	$ —	$ (209,000)	$ 333,000

Immediately preceding the launch of *AzaSite,* we offered wholesalers stocking incentives that allowed for extended payment terms, product discounts, and guaranteed sale provisions (collectively, "special terms"). These special terms were only offered during a specified time period of approximately one month prior to the August 13, 2007 launch of *AzaSite*. Any sales of *AzaSite* made under these special term provisions were

accounted for using a consignment model since substantially all the risks and rewards of ownership did not transfer upon shipment. Under the consignment model, we did not recognize revenue upon shipment of *AzaSite* purchased with the special terms, but recorded deferred revenue at gross invoice sales price, less all appropriate discounts and rebates, and accounted for *AzaSite* inventory held by the wholesalers as consignment inventory. We recognized the revenue from these sales with special terms at the earlier of when the inventory of *AzaSite* held by the wholesalers was sold through to the wholesalers' customers or when such inventory of *AzaSite* was no longer subject to these special terms. At December 31, 2007, we had net deferred revenue of $371,000 related to sales of *AzaSite* considered consignment, which was fully recognized in the three months ended March 31, 2008. All sales subsequent to this specified launch time period include return rights and pricing that are customary in the industry, as discussed above.

Product Co-promotion and Royalty Revenues

We recognize co-promotion revenue based on net sales of *Elestat* and royalty revenue based on net sales of *Restasis*, as defined in the co-promotion agreements, and as reported to us by Allergan. Through the year ended December 31, 2008, we actively promoted both *Restasis* and *Elestat* through our commercial organization. As of January 1, 2009, we are no longer responsible for the co-promotion of *Restasis*, but we continue to receive royalties on Allergan's net sales of *Restasis*. Our co-promotion and royalty revenues are based upon Allergan's revenue recognition policy and other accounting policies over which we have limited or no control and on the underlying terms of our co-promotion agreements. Allergan recognizes revenue from product sales when goods are shipped and title and risk of loss transfers to the customer. The co-promotion agreements provide for gross sales to be reduced by estimates of sales returns, credits and allowances, normal trade and cash discounts, managed care sales rebates and other allocated costs as defined in the agreements, all of which are determined by Allergan and are outside our control. We record a percentage of Allergan's reported net sales to us for *Elestat* and *Restasis,* as co-promotion revenue and royalty revenue, respectively. We receive monthly net sales information from Allergan and perform analytical reviews and trend analyses using prescription information that we receive from IMS Health. In addition, we exercise our audit rights under the contractual agreements with Allergan to annually perform an examination of Allergan's sales records of both *Restasis* and *Elestat*. We make no adjustments to the amounts reported to us by Allergan other than reductions in net sales to reflect the incentive programs managed by us. We offer and manage certain incentive programs associated with *Elestat*, which are utilized by us in addition to those programs managed by Allergan. We reduce co-promotion revenue from net sales of *Elestat* by estimating the portion of sales that are subject to these incentive programs based on information reported to us by our third-party administrator of the incentive programs. The rebates associated with the programs we manage represent an insignificant amount, as compared to the rebate and discount programs administered by Allergan and as compared to our aggregate co-promotion and royalty revenue. Under the co-promotion agreement for *Elestat*, we are obligated to meet predetermined minimum calendar year net sales target levels. If the annual minimum is not achieved, we record revenues using a reduced percentage of net sales based upon our level of achievement of the predetermined calendar year net sales target levels. Amounts receivable from Allergan in excess of recorded co-promotion revenue are recorded as deferred revenue. Calendar year 2009 was the last year in which there is a minimum annual net sales target level for *Elestat* under the co-promotion agreement.

Collaborative Research and Development Revenues

We recognize revenue under our collaborative research and development agreements when we have performed services under such agreements or when we or our collaborative partner have met a contractual milestone triggering a payment to us. We recognize revenue from our research and development service agreements ratably over the estimated service period as related research and development costs are incurred and the services are substantially performed. Upfront non-refundable fees and milestone payments received at the initiation of collaborative agreements for which we have an ongoing research and development commitment are deferred and recognized ratably over the period in which the services are substantially performed. This period, if not defined in the collaborative agreement, is based on estimates by management and the progress towards

agreed upon development events as set forth in our collaborative agreements. These estimates are subject to revision as our development efforts progress and we gain knowledge regarding required additional development. Revisions in the commitment period are made in the period that the facts related to the change first become known. If the estimated service period is subsequently modified, the period over which the upfront fee or revenue related to ongoing research and development services is modified on a prospective basis. We are also entitled to receive milestone payments under our collaborative research and development agreements based upon the achievement of agreed upon development events that are substantively at-risk by our collaborative partners or us. This collaborative research and development revenue is recognized upon the achievement and acknowledgement of our collaborative partner of a development event, which is generally at the date payment is received from the collaborative partner or is reasonably assured. Accordingly, our revenue recognized under our collaborative research and development agreements may fluctuate significantly from period to period. No collaborative research and development revenue was recognized for the years ended December 31, 2009 and 2007. In the year ended December 31, 2008, we recognized $1.25 million of collaborative research and development revenue from Santen upon the completion of its Phase 3 clinical testing relating to its formulation of diquafosol tetrasodium.

Inventories

Our inventories are related to *AzaSite* and are valued at the lower of cost or market using the first-in, first-out (i.e., FIFO) method. Cost includes materials, labor, overhead, shipping and handling costs. Our inventories are subject to expiration dating. We regularly evaluate the carrying value of our inventories and provide valuation reserves for any estimated obsolete, short-dated or unmarketable inventories. Our determination that a valuation reserve might be required, in addition to the quantification of such reserve, requires us to utilize significant judgment. We base our analysis, in part, on the level of inventories on hand in relation to our estimated forecast of product demand, production requirements for forecasted product demand, expected market conditions and the expiration dates or remaining shelf life of inventories. As of December 31, 2009 and 2008, we had net reserves of $25,000 and $10,000, respectively, for potential overstocking.

Taxes

We account for uncertain tax positions in accordance with FASB authoritative guidance regarding the accounting for taxes. Significant management judgment is required in determining our provision for income taxes, deferred tax assets and liabilities and any valuation allowance recorded against net deferred tax assets. We have recorded a valuation allowance against all potential tax assets due to uncertainties in our ability to utilize deferred tax assets, primarily consisting of certain net operating losses carried forward, before they expire. The valuation allowance is based on estimates of taxable income in each of the jurisdictions in which we operate and the period over which our deferred tax assets will be recoverable.

Liabilities

We generally enter into contractual agreements with third-party vendors to provide research and development, manufacturing, and other services in the ordinary course of business. Many of these contracts are subject to milestone-based invoicing and services are completed over an extended period of time. We record liabilities under these contractual commitments when we determine an obligation has been incurred, regardless of the timing of the invoice. We monitor all significant research and development, manufacturing, sales and marketing and other service activities and the progression of work related to these activities. We estimate the underlying obligation for each activity based upon our estimate of the amount of work performed and compare the estimated obligation against the amount that has been invoiced. Because of the nature of certain contracts and related delay in the contract's invoicing, the obligation to these vendors may be based upon management's estimate of the underlying obligation. We record the larger of our estimated obligation or invoiced amounts for completed service. In all cases, actual results may differ from our estimate.

Stock-Based Compensation Expense

We recognize stock-based compensation expense in accordance with FASB authoritative guidance regarding the accounting for share-based payments, which requires us to measure compensation cost for share-based payment awards at fair value and recognize compensation expense over the service period for awards expected to vest. We utilize the Black-Scholes option-pricing model to value our awards and recognize compensation expense on a straight-line basis over the vesting periods of our awards. We consider many factors when estimating expected forfeitures, including types of awards, employee class, and historical experience. Our expected volatility is determined based on our own historical volatility. The estimation of share-based payment awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from our current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. Significant management judgment is also required in determining estimates of future stock price volatility, forfeitures and expected life to be used in the valuation of the options. Actual results, and future changes in estimates, may differ substantially from our current estimates.

Impact of Inflation

We do not believe that our operating results have been materially impacted by inflation during the past three years. However, we cannot assure that our operating results will not be adversely affected by inflation in the future. We will continually seek to mitigate the adverse effects of inflation on the costs of goods and services that we use through improved operating efficiencies and cost containment and periodic price increases for our product.

Results of Operations

Years Ended December 31, 2009, 2008 and 2007

Revenues

Total revenues were approximately $92.2 million for the year ended December 31, 2009, as compared to approximately $70.5 million for the year ended December 31, 2008, and approximately $48.7 million in 2007. The increase in 2009 revenue of approximately $21.7 million, or 31%, as compared to the same period in 2008, was primarily due to an increase in product revenue from net sales of *AzaSite*, as well as increased royalty revenue from net sales of *Restasis*. The increase in 2008 revenue of approximately $21.8 million, or 45%, was primarily due to product revenue from a full year of net sales of *AzaSite,* as well as increased co-promotion revenue from net sales of *Restasis*, partially offset by a decrease in co-promotion revenue from net sales of *Elestat*. In addition, total revenues for the 2008 period included the recognition of a development milestone of $1.25 million from Santen for its development of diquafosol tetrasodium in accordance with our development, license and supply agreement, as previously discussed in this report.

Product Sales, net

Product sales of *AzaSite,* net of rebates and discounts, for the year ended December 31, 2009 were approximately $35.0 million, as compared to approximately $18.3 million in 2008 and approximately $3.1 million in 2007. *AzaSite* was launched by us in August 2007. The increase in 2009 revenue for *AzaSite* of approximately $16.7 million, or 91%, as compared to 2008, was primarily due to increased patient and physician usage of *AzaSite*, evidenced by an increase of prescriptions year-over-year, as well as a price increase for the product between the periods. Approximately $3.0 million to $4.0 million of revenue from sales of *AzaSite* for the year ended December 31, 2009 was associated with hospital usage of *AzaSite* as a substitute therapy during a temporary supply shortage of erythromycin ophthalmic ointment (0.5%), as discussed below.

In September 2009, erythromycin ophthalmic ointment was placed on the FDA Drug Shortages website. Erythromycin ophthalmic ointment is a macrolide antibiotic routinely used in neonates for prophylaxis of

ophthalmia neonatorum, a form of bacterial conjunctivitis that may be contracted by newborns during delivery. Due to this shortage, the Centers for Disease Control and Prevention (CDC) asked healthcare professionals to reserve erythromycin supplies for neonatal use and also recommended the use of *AzaSite* as an acceptable substitute for neonatal prophylaxis use when erythromycin was not available. We expect the erythromycin supply shortage to be resolved in the first quarter of 2010 and future use of *AzaSite* for neonatal use, as described above, to be limited.

The increase in AzaSite revenues in 2009 as compared to 2008 was partially offset by an increase in gross-to-net sales deductions. Total sales deductions as a percentage of gross revenues increased approximately 8%. The increase was primarily attributable to an increase in rebates associated with (1) an increase in the number of formularies that now list *AzaSite* and (2) the price concessions required to secure this coverage under Medicare and commercial managed care organizations. Additionally, we incurred an increase in IMA fee rates to wholesalers. The impact of these increases in coverage and IMA fee rates was approximately $3.6 million in additional provisions in 2009.

For the year ended December 31, 2009, based on prescription data from IMS Health, there were approximately 529,000 prescriptions written for *AzaSite,* excluding hospital usage, representing approximately 4% of all prescriptions in the single agent ocular anti-infective market, defined as both branded and generic single-entity ocular antibiotics. In comparison, approximately 303,000 prescriptions were written for *AzaSite* in 2008, representing approximately 2% of all prescriptions in the single agent ocular anti-infective market. In addition, our market share in our primary call audience of eye care specialists, mainly ophthalmologists and optometrists, was approximately 11% as of December 31, 2009, as compared to approximately 7% as of December 31, 2008. Since launch, actual units of *AzaSite* dispensed have been slightly higher than the number of prescriptions as reported by IMS Health due to the issuance of multiple unit prescriptions by some physicians. For the year ended December 31, 2009, the single agent ocular anti-infective market, in terms of prescriptions, was relatively unchanged from the prior year.

In July 2007, we started receiving and processing orders for *AzaSite* as part of the initial stocking of the supply chain. These initial orders were offered with special terms as stocking incentives for wholesalers. Sales with these special terms were accounted for using the consignment model, which requires that we defer revenue until such time that the product is resold further into the supply chain or the product is no longer subject to the special terms. As a result, as of December 31, 2007, approximately $371,000 of net *AzaSite* revenues were deferred and subsequently recognized in the first quarter of 2008. Sales made subsequent to this specified launch time period include return rights that are customary in the industry. For these orders, we are recording revenue at the date of shipment, when title and substantially all the risks and rewards of ownership has transferred to the customer.

Product Co-Promotion and Royalty

Total co-promotion and royalty revenue for the year ended December 31, 2009 was approximately $57.2 million, as compared to approximately $50.9 million in 2008 and approximately $45.5 million in 2007.

Our royalty revenue from net sales of *Restasis* for the year ended December 31, 2009 was approximately $38.4 million, as compared to approximately $32.8 million in 2008 and approximately $24.4 million in 2007. On December 24, 2008, we amended our agreement with Allergan such that we ceased co-promoting *Restasis* as of December 31, 2008. Notwithstanding the fact that we are no longer co-promoting *Restasis*, Allergan remains obligated to pay us royalties in relation to net sales of *Restasis* at the rates in effect prior to the December 2008 amendment. For the years ended December 31, 2009, 2008 and 2007, Allergan recorded revenue from net sales of *Restasis* of approximately $523 million, $444 million and $345 million, respectively.

The increase in both 2009 and 2008 royalty revenue for *Restasis*, as compared to 2008 and 2007, respectively, was primarily due to increased patient usage of *Restasis* and an increase in prescribers of *Restasis,* as evidenced by an increase in prescriptions year-over-year. In addition, there were annual price increases in the first quarters of 2009 and 2008.

Co-promotion revenue from net sales of *Elestat* for the year ended December 31, 2009 was approximately $18.8 million, as compared to approximately $18.1 million in 2008 and approximately $21.1 million in 2007. The increase in co-promotion revenue from net sales of *Elestat* of $615,000, or 3%, as compared to 2008, was primarily due to an annual price increase that became effective in the first quarter of 2009, partially offset by a slight decrease in the total U.S. allergic conjunctivitis market in 2009. The decrease in 2008 co-promotion revenue from net sales of *Elestat* of $3.0 million, as compared to 2007, was primarily due to a decline in the U.S. allergic conjunctivitis market in terms of prescriptions as well as a decline in *Elestat's* market share based on national prescription data as provided by IMS Health. This decrease was partially offset by an annual price increase for *Elestat* that became effective during the first quarter of 2008.

Elestat is a seasonal product with product demand mirroring seasonal trends for topical allergic conjunctivitis products. Typically, demand is highest during the Spring months followed by moderate demand in the Summer and Fall months. The lowest demand is during the Winter months. Based upon national prescription data from IMS Health, for the years ended December 31, 2009, 2008 and 2007, *Elestat* prescriptions, as a percentage of the total U.S. allergic conjunctivitis market, represented approximately 7%, 7% and 9%, respectively, of the total U.S. allergic conjunctivitis market. Subject to the entry of a generic epinastine product as discussed below, based on current trends in prescriptions for *Elestat,* we expect our 2010 market share to remain relatively constant with 2009 or slightly decrease. Based upon monthly data from IMS Health, the total U.S. allergic conjunctivitis market, in terms of prescriptions as compared to the previous year, decreased approximately 1%, 6% and 3%, respectively, for the years ended December 31, 2009, 2008 and 2007, respectively.

During the third quarter of 2009, ISTA Pharmaceuticals, Inc. received FDA approval for *Bepreve*™ (bepotastine besilate ophthalmic solution) 1.5% as a twice-daily prescription eye drop treatment for ocular itching associated with allergic conjunctivitis, and began commercializing this product in October 2009.

Under our agreement with Allergan related to our co-promotion of *Elestat,* prior to 2010, we were obligated to meet predetermined minimum calendar year net sales target levels, which increased annually. We were entitled to an escalating percentage of net sales of *Elestat* based upon predetermined calendar year net sales target levels. During a fiscal year, we recognized product co-promotion revenue associated with targeted net sales levels for *Elestat* achieved during that time period and deferred revenue in excess of the sales level achieved. Under the co-promotion agreement with Allergan, calendar year 2009 was the last year that our co-promotion revenues of *Elestat* are subject to annual minimum target levels.

Subject to applicable law, competitors are permitted to submit to the FDA an ANDA for a generic version of *Elestat*, due to the expiration of the marketing exclusivity period for *Elestat* provided under the Hatch-Waxman Act on October 15, 2008.

We have been notified that Boehringer Ingelheim and Allergan received notices from four companies: Apotex, Inc., Cypress Pharmaceutical, Inc., Paddock Laboratories, Inc., and Sandoz Inc., advising that each company filed an ANDA for a generic version of *Elestat*. The date of submission of the first filing to the FDA Office of Generic Drugs was October 14, 2008, according to the FDA's website (www.fda.gov). Furthermore, we have been notified by Allergan that Boehringer Ingelheim has decided not to file infringement lawsuits against the ANDA filers. Boehringer Ingelheim is the owner of a method of treatment patent related to *Elestat,* and we do not have a license to this patent.

The *Elestat* co-promotion agreement provides that unless earlier terminated, the term of such agreement will be in effect until the earlier of (i) the approval and launch of the first generic epinastine product after expiration of the FDA exclusivity period covering *Elestat* in the United States, or (ii) the approval and launch of the first over-the-counter epinastine product after expiration of the listing of *Elestat* in the FDA's Orange Book. Following the termination of such co-promotion agreement, we will no longer have rights to co-promote *Elestat.* We will be entitled to receive post-termination payments from Allergan, based on any remaining net sales of

Elestat for a period of 36 months. During the three successive 12-month periods immediately following the termination of the agreement, Allergan will be obligated to pay to us 20%, 15% and 10%, respectively, on any net sales of *Elestat* in the United States. We expect any revenue from net sales of *Elestat* received during this 36-month post-termination period to be minimal. We plan to continue co-promoting and receiving co-promotion revenues on *Elestat* sales during the FDA's review period of these ANDAs. We do not know when the FDA will complete its review but we expect that a generic form of epinastine could be launched in the second half of 2010. Loss of our co-promotion revenue from *Elestat* will significantly impact our results of operations and cash flows.

Collaborative Research and Development

In May 2008, Santen completed its Phase 3 clinical testing of diquafosol tetrasodium in Japan, which it refers to as DE-089, for which we received a milestone payment of $1.25 million. We did not receive any collaborative research and development revenue during 2009 or 2007. Santen is responsible for all development, regulatory submissions, filings and approvals, and the commercialization of potential products in Japan and nine other Asian countries. We could receive additional development milestone payments from Santen of up to $1.75 million, as well as royalties on net sales of diquafosol tetrasodium, if the product candidate is approved for commercialization in Santen's licensed territories. Santen filed an application for manufacturing and marketing approval of DE-089 with the Japanese Ministry of Health, Labor, and Welfare (the Japanese equivalent of the FDA) on May 30, 2008, which is pending review.

Our future revenue will depend on various factors including the effectiveness of our commercialization of *AzaSite* and continued commercial success and duration of commercial exclusivity of *Restasis* and *Elestat.* In addition to the foregoing, pricing, rebates, discounts and returns for all products; the effect of competing products; coverage and reimbursement under commercial or government plans; and seasonality of sales of *Elestat* will impact future revenues. If Allergan significantly under-estimates or over-estimates rebate amounts, there could be a material effect on our revenue. In addition to the continuing sales of *AzaSite*, *Restasis* and *Elestat*, our future revenue will also depend on our ability to enter into additional collaboration agreements, and to achieve milestones under existing or future collaboration agreements, as well as whether we obtain regulatory approvals for our product candidates.

Cost of Sales

Cost of sales related to the sales of *AzaSite* were approximately $11.3 million for the year ended December 31, 2009, as compared to approximately $6.4 million in 2008 and approximately $1.6 million in 2007. The increase in cost of sales of $4.9 million, or 76%, as compared to 2008, was primarily due to increased sales volume of *AzaSite,* which has resulted in increased royalties, as well as an increase in the royalty rate, paid to InSite Vision. Through June 30, 2009, we paid a 20% royalty to InSite Vision on net sales of *AzaSite* in accordance with our licensing agreement. In July 2009, our royalty rate to InSite Vision on net sales of *AzaSite* increased from 20% to 25% and will remain at 25% for the remaining term of the licensing agreement.

Cost of sales expense consists of variable and fixed cost components. Variable cost components include royalties to InSite Vision on net sales of *AzaSite*, the cost of *AzaSite* inventory sold, distribution, shipping and logistic service charges from our third-party logistics provider, and changes to our inventory reserve for overstocking or short-dated material. Fixed cost components are primarily the amortization of the $19.0 million approval milestone that we paid InSite Vision as part of our licensing agreement. This approval milestone is being amortized ratably on a straight-line basis through the term of the underlying patent coverage for *AzaSite*, which expires in March 2019.

Certain costs included in cost of sales are subject to annual increases for which we have limited control. We expect that cost of sales will increase in relation to, but not proportionately to, the increases in revenue from sales of *AzaSite.*

Costs and Expenses

Research and Development Expenses

Research and development expenses were approximately $51.1 million for the year ended December 31, 2009, as compared to approximately $44.6 million in 2008 and approximately $53.4 million in 2007.

The increase in research and development expenses of approximately $6.5 million, or 15%, for the year ended December 31, 2009, as compared to 2008, was primarily due to increased costs associated with our cystic fibrosis program, including the recognition of an approximate $3.3 million milestone payable to Yamasa Corporation upon entering into an agreement to license certain technology related to manufacturing in support of this program. Effective September 25, 2009, we entered into a technology license agreement with Yamasa Corporation to facilitate the transfer of the current denufosol manufacturing technology, including intellectual property, to an additional manufacturer and thus enable a two-supplier strategy for denufosol. The remaining increase in research and development expenses was due to the initiation of a Phase 2 program for *AzaSite* for the treatment of blepharitis.

These increases in research and development expenses for the year ended December 31, 2009 were partially offset by reduced spending on our glaucoma program as a result of the completion of Phase 1 trial activities, the discontinuation of our program for the development of epinastine nasal spray for allergic rhinitis in 2008, and cost savings from our restructuring activities in the first quarter of 2009.

The decrease in research and development expenses of approximately $8.8 million, or 16%, for the year ended December 31, 2008, as compared to 2007, was primarily due to a one-time $13.0 million upfront *AzaSite* licensing fee paid in 2007 which did not occur in 2008. Excluding this one-time fee, our research and development expenses associated with our other product candidates increased approximately $4.2 million for the year ended December 31, 2008, as compared to 2007, and was primarily due to increased activities associated with our cystic fibrosis and glaucoma product candidates. Additionally, we incurred a general increase in annual salaries, personnel related expenses and stock-based compensation expense. See Part I—Item 1. Business of this report for a detailed development status of these programs.

Research and development expenses include all direct and indirect costs, including salaries for our research and development personnel, consulting fees, clinical trial costs, including the development and manufacture of drug product for clinical trials, sponsored research costs, clinical trial insurance, upfront license fees, milestone and royalty payments relating to research and development, and other fees and costs related to the development of product candidates. Research and development expenses vary according to the number of programs in clinical development and the stage of development of our clinical programs. Later stage clinical programs tend to cost more than earlier stage programs due to the length of the clinical trials and the number of patients enrolled in later stage clinical trials.

Our future research and development expenses will depend on the results and magnitude or scope of our clinical activities and requirements imposed by regulatory agencies. Year over year spending on active development programs can vary due to the differing levels and stages of development activity, the timing of certain expenses and other factors. Accordingly, our research and development expenses may fluctuate significantly from period to period. In addition, if we in-license or out-license rights to product candidates, our research and development expenses may fluctuate significantly from prior periods.

Our research and development expenses for the years ended December 31, 2009, 2008 and 2007 and from the respective project's inception are shown below and includes the percentage of overall research and development expenditures for the years listed.

	(In thousands) Year ended December 31,						Cumulative from Inception to December 31, 2009	
	2009	%	2008	%	2007	%		%
Denufosol tetrasodium for cystic fibrosis [1]	$29,590	58	$18,633	42	$13,599	25	$ 94,370	26
Prolacria (diquafosol tetrasodium) for dry eye disease	6,621	13	7,632	17	4,181	8	57,572	16
AzaSite for blepharitis	6,297	12	83	—	—	—	6,380	2
INS115644 and INS117548 for glaucoma and related research and development	1,555	3	5,552	12	5,235	10	16,447	5
Epinastine nasal spray for allergic rhinitis [2]	40	—	3,383	8	7,991	15	19,889	5
AzaSite [3]	2,311	5	1,621	4	14,598	27	18,530	5
Other research, preclinical and development costs [4]	4,720	9	7,733	17	7,787	15	150,787	41
Total	$51,134	100	$44,637	100	$53,391	100	$363,975	100

(1) Includes the recognition of an approximate $3.3 million milestone in September 2009.

(2) In April 2008, we discontinued the development of epinastine nasal spray.

(3) Expense in 2007 includes a $13.0 million upfront licensing fee upon the signing of the license agreement with InSite Vision.

(4) Prior to February 2009, other research, preclinical and development costs represent all unallocated research and development costs or those costs allocated to preclinical programs as well as costs of discontinued and/or inactive programs. These unallocated costs included personnel costs of our research, preclinical programs, internal and external general research costs and other internal and external costs of other research, preclinical and development programs. In February 2009, we restructured our operations eliminating our preclinical and molecule discovery activities.

Selling and Marketing Expenses

Selling and marketing expenses were approximately $49.3 million for the year ended December 31, 2009, as compared to approximately $54.6 million in 2008 and approximately $45.5 million in 2007.

The decrease in selling and marketing expenses of approximately $5.3 million, or 10%, for the year ended December 31, 2009, as compared to 2008, was due to an overall reduction in promotional and marketing activities, including Phase 4 clinical trial activities, partially offset by a general increase in personnel related expenses, including stock-based compensation expense.

The increase in selling and marketing expenses of approximately $9.1 million, or 20%, for the year ended December 31, 2008, as compared to 2007, resulted from an overall increase in various expenses primarily associated with the full year commercialization of *AzaSite*, including a full year of expenses related to our expanded sales force and managed markets group. Additionally, we had increased marketing and promotional activities and Phase 4 program costs in 2008. We also incurred a general increase in annual salaries, personnel related expenses and stock-based compensation expense.

Our commercial organization currently focuses its promotional efforts on approximately 9,000 eye care specialists. Our selling and marketing expenses include all direct costs associated with the commercial

organization, which include our sales force and marketing programs. Our sales force expenses include salaries, training and educational program costs, product sample costs, fleet management and travel. Our marketing and promotion expenses include product management, promotion, advertising, public relations, Phase 4 clinical trial costs, physician training and continuing medical education and administrative expenses. We adjust the timing, magnitude and targeting of our advertising, promotional, Phase 4 clinical trials and other commercial activities for our products based on seasonal trends and other factors, and accordingly, these costs can fluctuate from period to period.

Future selling and marketing expenses will depend on the level of our future commercialization activities. We expect selling and marketing expenses will increase in periods that immediately precede and follow product launches. In addition, if we in-license or out-license rights to products, our selling and marketing expenses may fluctuate significantly from prior periods.

General and Administrative Expenses

General and administrative costs were approximately $16.1 million for the year ended December 31, 2009, as compared to approximately $14.5 million in 2008 and approximately $14.0 million in 2007.

The increase in general and administrative expenses of approximately $1.5 million, or 10%, for the year ended December 31, 2009, as compared to 2008, was primarily due to an increase in consulting and legal expenses, as well as an increase in personnel related expenses and stock-based compensation. These increases were partially offset by a final reimbursement of legal fees in 2009 received from our insurance provider of approximately $875,000 related to our stockholder litigation and SEC investigation.

The increase in general and administrative expenses of approximately $554,000, or 4%, for the year ended December 31, 2008, as compared to 2007, was primarily due to a general increase in annual salaries, personnel related expenses and stock-based compensation expense as well as an increase in legal and administrative expenses associated with our stockholder litigation and SEC investigation. These increases were partially offset by a reduction in consulting fees during 2008. In addition, general and administrative expenses for 2007 include a large initial reimbursement of legal fees received from our insurance provider related to our stockholder litigation and SEC investigation.

On September 30, 2008, the SEC approved a non-monetary settlement of the previously announced investigation of Inspire and two of our officers by the SEC staff relating to our disclosures regarding a Phase 3 clinical trial of our dry eye product candidate, *Prolacria*.

On July 26, 2007, the United States District Court for the Middle District of North Carolina granted Inspire's and the other defendants' motion and dismissed the previously announced Consolidated Class Action Complaint with prejudice. On December 12, 2008, the Fourth Circuit of the Unites States Court of Appeals issued an opinion affirming the judgment of the District Court.

Our general and administrative expenses consist primarily of personnel, facility and related costs for general corporate functions, including business development, finance, accounting, legal, human resources, quality/ compliance, facilities and information systems.

Future general and administrative expenses will depend on the level and extent of support required to conduct our future research and development, commercialization, business development, and corporate activities.

Restructuring

In March 2009, we announced that we had restructured our operations during the first quarter of 2009, eliminating preclinical and drug discovery activities and refocusing our resources on the development of existing

later-stage clinical programs and commercially available products. In connection with the restructuring, we recorded restructuring charges of approximately $2.0 million for the year ended December 31, 2009, which are reported in a separate line item in our Statement of Operations. Significant components of the restructuring charge were one-time termination benefits for employees impacted by the restructuring, estimated costs to write-down idle lab equipment to net realizable value, losses associated with leased lab space that is now vacant, and costs to satisfy contract commitments related to activities and programs no longer associated with our supported programs and on-going operations. As a result of this restructuring, cost savings for 2009 were approximately $3 million to $3.5 million.

Other Income (Expense)

For the year ended December 31, 2009, we incurred other expense, net of approximately $2.4 million, as compared to approximately $1.9 million in other expense, net in 2008 and approximately $2.1 million in other income, net in 2007.

The increase in other expense, net of approximately $415,000 for the year ended December 31, 2009, as compared to 2008, was due to decreased interest income partially offset by a decrease in interest expense. Interest income was negatively impacted due to lower average cash and investment balances combined with a lower rate of return during 2009, as compared to 2008. The decrease in interest expense is the result of a lower average outstanding principal balance of our term loan facility during 2009, as compared to 2008.

The decrease in other income of approximately $4.0 million for the year ended December 31, 2008, as compared to 2007, was due to a combination of decreased interest income and increased interest expense. Interest income was negatively impacted due to a lower rate of return on our cash and investments as well as lower average cash and investment balances in 2008 compared to 2007. The increase in interest expense was associated with additional borrowings of an aggregate of $40.0 million during 2007 under our term loan facility.

Other income/(expense) fluctuates from year to year depending on the level of interest income earned on variable cash and investment balances, realized gains and losses on investments due to changes in fair market value and interest expense on debt and capital lease obligations. Future other income/(expense) will depend on our future cash and investment balances, the return and change in fair market value on these investments, as well as levels of debt and the associated interest rates.

Liquidity and Capital Resources

We have financed our operations primarily through the sale of equity securities, including private sales of preferred stock and public offerings of common stock and, to a lesser extent, through our term loan facility. We also currently receive co-promotion revenue from net sales of *Elestat,* royalty revenue from net sales of *Restasis*, and product revenue from net sales of *AzaSite*. We do not expect our revenue to exceed our operating expenses in 2010.

At December 31, 2009, we had net working capital of approximately $85.4 million, an increase of approximately $32.9 million from approximately $52.5 million at December 31, 2008. The increase in working capital was principally due to the sale of common stock described below, offset by the funding of normal operating expenses associated with commercialization activities and the development of our product candidates, as well as principal and interest payments on our term loan facility. Our principal sources of liquidity at December 31, 2009 were approximately $52.3 million in cash and cash equivalents, approximately $76.0 million in investments, which are considered available-for-sale, and approximately $22.7 million in trade receivables.

In August 2009, we completed a public offering of 25,555,555 shares of our common stock at a price of $4.50 per share, which included an additional 3,333,332 shares underwriter over-allotment option, for gross proceeds of $115 million. Net proceeds were $109 million, after deducting underwriting discounts and offering expenses.

In July 2007, we completed a sale of preferred stock to Warburg pursuant to which we sold 140,186 shares of our Exchangeable Preferred Stock at a price per share of $535.00, for net proceeds of $73.6 million. The Exchangeable Preferred Stock was exchanged for 14,018,600 shares of common stock on October 31, 2007.

In December 2006, we entered into a loan and security agreement in order to obtain debt financing of up to $40.0 million to fund in-licensing opportunities and related development. In June 2007, we amended the loan and security agreement to enable us to draw upon a new supplemental term loan facility in the amount of $20.0 million. We have borrowed the full $60.0 million under the term loan facility of which $25.2 million remained outstanding as of December 31, 2009. We make scheduled principal and interest payments on a monthly basis and all loan advances made under the agreement have a final maturity date in March 2011. See Note 9 "Debt" to our financial statements for further discussion regarding the term loan facility.

In March 2009, we announced that we had restructured our operations during the first quarter of 2009, eliminating preclinical and drug discovery activities and refocusing our resources on the development of existing later-stage clinical programs and commercially available products. As a result of this restructuring, we expect to eliminate future cash expenditures of approximately $6 million on an annual basis subsequent to 2009.

Our working capital requirements may fluctuate in future periods depending on many factors, including: the number, magnitude, scope and timing of our development programs; the commercial potential and success of our products; the potential loss of commercial exclusivity of any of our products; the loss of revenue from our products due to competition or loss of market share; the level of ongoing costs related to the commercialization of *AzaSite* and *Elestat;* the costs related to the potential FDA approval of our other product candidates; the cost, timing and outcome of regulatory reviews, regulatory investigations, and changes in regulatory requirements; the costs of obtaining patent protection for our product candidates; the timing and terms of business development activities; the rate of technological advances relevant to our operations; the timing, method and cost of the commercialization of our product candidates; the efficiency of manufacturing processes developed on our behalf by third parties; the level of required administrative support for our daily operations; the availability of capital to support product candidate development programs we pursue; and the commercial potential of our product candidates.

2010 Financial Guidance

Based upon current trends and assumptions, we expect to record 2010 aggregate revenue in the range of $100-$111 million. Co-promotion revenue from net sales of *Elestat* will be dependent upon the timing of a launch of a generic form of epinastine which we expect may occur in the second half of 2010. Furthermore, hospital usage of *AzaSite* is expected to decline significantly due to the resolution of the supply shortage of erythromycin ophthalmic ointment (0.5%) in the first quarter of 2010. Total 2010 operating expenses are expected to be in the range of $145-$169 million based on our planned activities. Cost of sales, which includes the amortization of the *AzaSite* approval milestone and royalty obligations to InSite Vision, is expected to be in the range of $13-$18 million. Total estimated selling and marketing and general and administrative expenses are estimated to be in the range of $48-$53 million and $27-$32 million, respectively. Research and development expenses are estimated to be in the range of $60-$70 million. Included within this operating expense guidance are projected stock-based compensation costs of approximately $8-$12 million. Due to expense associated with our CEO transition, primarily stock-based compensation expense, we expect the first quarter 2010 general and administrative expenses to be the largest as compared to the remaining quarters of 2010. In addition, a significant portion of our promotional activities usually occur during the first quarter of each year. As a result, we expect that the first quarter commercial expenses will be the largest of 2010.

Our ability to remain within our operating expense target range is subject to multiple factors, including unanticipated cost overruns, the need to expand or reduce the magnitude or scope of existing development programs, the need to change the number or timing of clinical trials, unanticipated regulatory requirements, unanticipated costs to successfully commercialize our products and product candidates, the commercial success of our current products and other factors described under the Risk Factors located elsewhere in this report.

Operating cash utilization in 2010 is expected to be in the range of $58-$73 million, which incorporates $20 million of principal repayment on our outstanding debt. Our need for additional working capital will largely be determined by the commercial success of our products and the successful and timely completion of our development programs. In order for us to continue operations substantially beyond 2010 we will need to: (1) successfully increase revenues, (2) obtain additional product candidate approvals, (3) out-license rights to certain of our product candidates, (4) raise additional capital through equity or debt financings or from other sources, (5) reduce spending on one or more research and development programs and/or (6) further restructure our operations. Additionally, after deducting the $115 million of common stock sold in August 2009, we retain the ability to offer for sale $15 million of securities, including common stock, preferred stock, debt securities, depositary shares and securities warrants from an effective shelf registration statement which we filed with the SEC on March 9, 2007. The loan and security agreement that we entered into in December 2006, as amended in June 2007, contains a financial covenant that requires us to maintain certain levels of liquidity based on our cash, investment and account receivables balances, as well as negative covenants that may limit us from assuming additional indebtedness and entering into other transactions as defined in the agreement. The agreement also includes a subjective acceleration clause which provides our lenders with the ability to accelerate repayment, even if we are in compliance with all conditions of the agreement, upon a material adverse change to our business, properties, assets, financial condition or results of operations. At December 31, 2009, we were in compliance with all of the covenants under our loan and security agreement and project that we will be throughout 2010.

Contractual Obligations and Commitments

In the normal course of business, we enter into various agreements that create contractual obligations and commitments that may require future cash payments. Contractual obligations at December 31, 2009 included operating leases of $2.6 million, long-term borrowings of $25.2 million, interest payments of $1.4 million, and purchase obligations and other commitments, as further described below.

As part of our drug development strategy, we outsource significant amounts of our preclinical and clinical programs and the manufacture of drug substance used in those programs. In addition, we have manufacturing, promotion and clinical responsibilities and activities associated with the commercialization of *AzaSite*. Based on these requirements and activities, we have entered into contractual commitments or purchase obligations with various clinical research organizations, promotion and advertising agencies, manufacturers of active pharmaceutical ingredients and drug product for clinical and commercial use as well as with others. These financial commitments, which totaled approximately $17.5 million as of December 31, 2009, are reflected as purchase obligations in the table below and include both cancelable and non-cancelable arrangements. Since many of these commitment amounts are dependent upon variable components of the agreements, actual payments and the timing of those payments may differ from management's estimates.

The terms of our existing license, collaboration and sponsored research agreements may require that we make cash payments contingent upon the occurrence of certain future events. In the aggregate, these agreements may require payments of up to $21.4 million assuming the achievement of all development milestones and up to an additional $4.0 million assuming the achievement of all sales milestones. Amounts payable by us under these agreements are uncertain and are contingent on a number of factors, including the progress of our research, preclinical and development programs, our ability to obtain regulatory approvals, the commercial success of our approved products and future annual product sales levels.

If certain of our product candidates are approved by the FDA and are subsequently commercialized, we will be obligated to pay royalties on net sales of the commercialized products. See Part I—Item 1. Business—Collaborative Agreements of this report for a full discussion of our royalty obligations under our in-licensing agreement with Wisconsin Alumni Research Foundation for our glaucoma product candidates. In addition, we are obligated to pay royalties to InSite Vision as part of our in-licensing agreement for *AzaSite*. Under the terms of the agreement, our obligation to pay royalties to InSite Vision is subject to pre-determined minimum annual

royalty payments. The determination of whether or not we will owe any such payments is based upon the amount of royalties accrued over a 12-month royalty period. There are five successive 12-month minimum royalty periods, the first of which commenced on October 1, 2008. The minimum royalties escalate each year. Remaining minimum royalties as of December 31, 2009 total $60.0 million.

The table below reflects contractual and potential obligations as of December 31, 2009. Some of the figures we include in this table are based on management's estimate and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties, and other factors as previously described. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table:

	(In thousands) Payment due by Period as of December 31, 2009				
Contractual and Potential Obligations	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Debt Obligations	$ 25,175	$19,940	$ 5,235	$ —	$ —
Interest on Debt Obligations	1,350	1,280	70	—	—
Operating Lease Obligations [1]	2,626	1,751	875	—	—
Purchase Obligations [2]	17,489	15,195	2,294	—	—
Minimum Annual License Payments	25	25	—	—	—
Development Milestone Obligations [3][4]	21,350	3,250	7,950	4,800	5,350
Minimum Royalties and Sales Milestone Obligations [4]	64,000	9,000	32,000	19,000	4,000
Total	$132,015	$50,441	$48,424	$23,800	$9,350

(1) Includes estimated payments of $1,219 for the cancelable portion of operating leases, primarily our fleet vehicles under a master lease agreement. See Note 14, "Commitments and Contingencies" for a full discussion.

(2) Purchase obligations reflect all contractual obligations, including amounts that are cancelable, under legally enforceable contracts with contract terms that are both fixed and determinable. These amounts exclude obligations for goods and services that already have been incurred and are reflected on our Balance Sheet as of December 31, 2009.

(3) Includes $1.9 million of "other long-term liabilities" as recorded on our Balance Sheet as of December 31, 2009.

(4) Development and sales milestone obligations represent potential amounts payable by us contingent on a number of factors, including the progress of our research, preclinical and development programs, our ability to obtain regulatory approvals, and the commercial success of our approved products.

Impact of Recently Issued Accounting Pronouncements

In January 2010, the FASB issued authoritative guidance for improving disclosures about fair value measurements. This guidance requires some new disclosures and clarifies some existing disclosure requirements about fair value measurement. The new disclosure requirements are effective for interim and annual reporting periods beginning after December 15, 2009, except for the disclosures about purchases, sales, issuances, and settlements in the roll forward of activity in Level 3 fair value measurements. Those disclosures are effective for fiscal years beginning after December 15, 2010, and for interim periods within those fiscal years. Since the new guidance only impacts financial statement disclosures, there will be no impact to our financial position or results of operations upon adoption.

In October 2009, the FASB issued authoritative guidance regarding revenue arrangements with multiple deliverables. The guidance requires entities to allocate revenue in an arrangement using estimated selling prices of the delivered goods and services based on a selling price hierarchy. The guidance further eliminates the

residual method of revenue allocation and requires revenue to be allocated using the relative selling price method. The new guidance should be applied on a prospective basis for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010, with early adoption permitted. We are currently assessing the impact of adopting this new guidance.

In August 2009, the FASB issued authoritative guidance regarding measuring liabilities at fair value. The authoritative guidance sets forth the types of valuation techniques to be used to value a liability when a quoted price in an active market for the identical liability is not available. It also clarifies transfer restrictions on the fair value of a liability and the ability to use the fair value of a liability that is traded as an asset as an input to the valuation of the underlying liability. The authoritative guidance is effective for interim and annual periods beginning after August 26, 2009. We have assessed the impact of this new guidance and expect no material impact to our financial statements upon adoption.

In May 2009, the FASB issued authoritative guidance regarding subsequent events. The authoritative guidance establishes general standards of accounting for and disclosure of events that occur after the balance sheet date but before financial statements are issued or are available to be issued. The authoritative guidance is effective for interim and annual periods ending after June 15, 2009.

In April 2009, the FASB issued authoritative guidance to aid in determining fair value when the volume and level of activity for the assets or liabilities have significantly decreased and when identifying transactions are not orderly, such as a forced liquidation or distressed sale. The authoritative guidance became effective for us on April 1, 2009 and the adoption of the guidance did not have a material impact on our consolidated financial statements.

In April 2009, the FASB issued authoritative guidance on the recognition and presentation of other-than-temporary impairments. The authoritative guidance incorporates impairment guidance for debt securities from various sources of authoritative literature and clarifies the interaction of the factors that should be considered when determining whether a debt security is other than temporarily impaired. The authoritative guidance became effective for us on April 1, 2009 and the adoption of the guidance did not have a material impact on our consolidated financial statements.

In April 2009, the FASB issued authoritative guidance to require disclosures about fair value of financial instruments in interim financial statements as well as in annual financial statements. The authoritative guidance is effective for interim periods ending after June 15, 2009, and we have adopted the guidance and have provided the additional disclosures as required.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

We are subject to interest rate risk on our investment portfolio and borrowings under our term loan facility.

We invest in marketable securities in accordance with our investment policy. The primary objectives of our investment policy are to preserve capital, maintain proper liquidity to meet operating needs and maximize yields. Our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment. Our investment portfolio may consist of a variety of securities, including United States government and government agency obligations, money market and mutual fund investments, municipal and corporate notes and bonds and asset or mortgage-backed securities. As of December 31, 2009, cash equivalents consisted of $6.4 million in a money market account and $36.1 million in money market funds and $5.0 million in a U.S. government agency security with a maturity less than 90 days. Our investment portfolio as of December 31, 2009 consisted of corporate notes and bonds, commercial paper, U.S. Government and agency securities, and negotiated certificates of deposit and had an average maturity of less than 12 months, using the stated maturity. All of our cash, cash equivalents and investments are maintained at two banking institutions.

Our investment exposure to market risk for changes in interest rates relates to the increase or decrease in the amount of interest income we can earn on our portfolio, changes in the market value due to changes in interest rates and other market factors as well as the increase or decrease in any realized gains and losses. Our investment portfolio includes only marketable securities and instruments with active secondary or resale markets to help ensure portfolio liquidity and we have implemented guidelines limiting the duration of investments. At December 31, 2009, our portfolio of available-for-sale investments consisted of approximately $54.4 million of investments maturing within one year and approximately $21.7 million of investments maturing after one year but within 24 months. In general, securities with longer maturities are subject to greater interest-rate risk than those with shorter maturities. A hypothetical 100 basis point drop in interest rates along the entire interest rate yield curve would not significantly affect the fair value of our interest sensitive financial instruments. We generally have the ability to hold our fixed-income investments to maturity and therefore do not expect that our operating results, financial position or cash flows will be materially impacted due to a sudden change in interest rates. However, our future investment income may fall short of expectations due to changes in interest rates, or we may suffer losses in principal if forced to sell securities which have declined in market value due to changes in interest rates or other factors, such as changes in credit risk related to the securities' issuers.

We do not use interest rate derivative instruments to manage exposure to interest rate changes. We ensure the safety and preservation of invested principal funds by limiting default risk, market risk and reinvestment risk. We reduce default risk by investing in investment grade securities.

Our risk associated with fluctuating interest expense is limited to future capital leases and other short-term debt obligations we may incur in our normal operations. The interest rates on our long-term debt borrowings under the term loan facility are fixed and as a result, interest due on borrowings are not impacted by changes in market-based interest rates.

Investment Risk

In addition to our normal investment portfolio, we have an investment in Parion Sciences, Inc. of $200,000 as of December 31, 2009. This investment is in the form of unregistered common stock and is subject to higher investment risk than our normal investment portfolio due to the lack of an active resale market for the Parion Sciences, Inc. securities.

Foreign Currency Exchange Risk

The majority of our transactions occur in U.S. dollars and we do not have subsidiaries or investments in foreign countries. Therefore, we are not subject to significant foreign currency exchange risk. We do, however, have foreign currency exposure with regard to the purchase of active pharmaceutical ingredients as they relate to *AzaSite*, which is manufactured by a foreign-based company, future milestone payments due under the technology license agreement with Yamasa Corporation, as well as development activities currently ongoing in Europe. We have established policies and procedures for assessing market and foreign exchange risk. As of December 31, 2009, we did not have any material foreign currency hedges.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. A list of the financial statements filed herewith is found at "Index to Financial Statements" on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

Not applicable.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management is responsible for establishing and maintaining an adequate system of internal control over our financial reporting. The design, monitoring and revision of the system of internal accounting controls involves, among other items, management's judgments with respect to the relative cost and expected benefits of specific control measures. The effectiveness of the control system is supported by the selection, retention and training of qualified personnel and an organizational structure that provides an appropriate division of responsibility and formalized procedures. The system of internal accounting controls is periodically reviewed and modified in response to changing conditions. Internal audit consultants regularly monitor the adequacy and effectiveness of internal accounting controls. In addition to the system of internal accounting controls, management maintains corporate policy guidelines that help monitor proper overall business conduct, possible conflicts of interest, compliance with laws and confidentiality of proprietary information. Our Chief Executive Officer and Chief Financial Officer have reviewed and evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Securities Exchange Act of 1934 as of the end of the period covered by this report. Based on that evaluation, the Chief Executive Officer and Chief Financial Officer have concluded that our current disclosure controls and procedures are effective.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting as defined in Rules 13a-15(f) and 15d-15(f) of the Securities Exchange Act of 1934, and for performing an assessment of the effectiveness of internal control over financial reporting as of December 31, 2009. 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. Our system of internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

Management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this evaluation, management, including our principal executive officer and principal financial officer, concluded that our internal control over financial reporting was effective as of December 31, 2009. The effectiveness of our internal control over financial reporting as of December 31, 2009 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which is presented in this Annual Report on Form 10-K.

Changes in Control Over Financial Reporting

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

Audit Committee Oversight

The Audit Committee of the Board of Directors, consisting solely of independent directors, appoints the independent registered public accounting firm and receives and reviews the reports submitted by them. The Audit

Committee meets several times during the year with management, the internal auditors and the independent registered public accounting firm to discuss audit activities, internal controls and financial reporting matters. The internal auditors and the independent registered public accounting firm have full and free access to the Audit Committee.

Item 9B. Other Information.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated by reference to the material responsive to this item contained in our Proxy Statement to be filed in connection with our 2010 Annual Meeting of Stockholders.

Item 11. Executive Compensation.

The information required by this item is incorporated by reference to the material responsive to this item contained in our Proxy Statement to be filed in connection with our 2010 Annual Meeting of Stockholders.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The following table sets forth certain information with respect to securities authorized for issuance under equity incentive plans as of December 31, 2009.

Equity Compensation Plan Information

Plan category	(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights	(b) Weighted-average exercise price of outstanding options, warrants and rights	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column(a))
Equity compensation plans approved by security holders	11,175,516	$7.47	1,284,708
Equity compensation plans not approved by security holders	0	0	0
Total	11,175,516	$7.47	1,284,708

The additional information required by this item is incorporated by reference to the material responsive to this item contained in our Proxy Statement to be filed in connection with our 2010 Annual Meeting of Stockholders.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item is incorporated by reference to the material responsive to this item contained in our Proxy Statement to be filed in connection with our 2010 Annual Meeting of Stockholders.

Item 14. Principal Accountant Fees and Services.

The information required by this item is incorporated by reference to the material responsive to this item contained in our Proxy Statement to be filed in connection with our 2010 Annual Meeting of Stockholders.

PART IV

Item 15. Exhibits and Financial Statements Schedules.

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

1. Financial Statements:

2. Financial Statement Schedule:

Schedule of Valuation and Qualifying Accounts
(in thousands)

	Beginning Balance	Additions: Charged to Costs and Expenses	Additions: Charged to Other Accounts	Deductions from Allowances	Ending Balance
Year ended December 31, 2007					
Allowance for rebates, chargebacks and other sales incentives	$ —	$ 366	$ 58	$ (186)	$ 238
Allowance for returns	—	105	13	(23)	95
Allowance for uncollectible accounts	—	10	—	—	10
Inventory allowance	—	125	—	—	125
Valuation allowance for income taxes	110,008	27,201	—	(4,000)[1]	133,209
Year ended December 31, 2008					
Allowance for rebates, chargebacks and other sales incentives	$ 238	$ 2,888	$—	$(1,824)	$ 1,302
Allowance for returns	95	677	—	(71)	701
Allowance for uncollectible accounts	10	—	—	(3)	7
Inventory allowance	125	105	—	(220)	10
Valuation allowance for income taxes	133,209	25,321	—	—	158,530
Year ended December 31, 2009					
Allowance for rebates, chargebacks and other sales incentives	$ 1,302	$ 9,531	$—	$(6,456)	$ 4,377
Allowance for returns	701	1,560	—	(738)	1,523
Allowance for uncollectible accounts	7	43	—	—	50
Inventory allowance	10	15	—	—	25
Valuation allowance for income taxes	158,530	19,629	—	—	178,159

(1) Deduction as a result of implementing FASB guidance on accounting for uncertainty in income taxes.

For additional information regarding the Company's reserves and allowances for rebates, chargebacks, discounts and returns, see—"Management's Discussion and Analysis of Financial Condition and Results of Operations—Revenue Recognition."

All other schedules are omitted as the information required is inapplicable or the information is presented in the financial statements.

3. Exhibits:

See the Exhibit Index located at the end of this document.

SIGNATURES

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

Inspire Pharmaceuticals, Inc.

By: /s/ ADRIAN ADAMS

Adrian Adams
President & Chief Executive Officer and Director

Date: March 15, 2010

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

Signature	Title	Date
/s/ ADRIAN ADAMS **Adrian Adams**	President & Chief Executive Officer (principal executive officer) and Director	March 15, 2010
/s/ THOMAS R. STAAB, II **Thomas R. Staab, II**	Chief Financial Officer & Treasurer (principal financial officer and principal accounting officer)	March 15, 2010
/s/ KENNETH B. LEE, JR. **Kenneth B. Lee, Jr.**	Chairman of the Board of Directors	March 15, 2010
/s/ GEORGE ABERCROMBIE **George Abercrombie**	Director	March 15, 2010
/s/ KIP A. FREY **Kip A. Frey**	Director	March 15, 2010
/s/ ALAN F. HOLMER **Alan F. Holmer**	Director	March 15, 2010
/s/ NANCY J. HUTSON **Nancy J. Hutson**	Director	March 15, 2010
/s/ JONATHAN S. LEFF **Jonathan S. Leff**	Director	March 15, 2010
/s/ RICHARD S. KENT **Richard S. Kent**	Director	March 15, 2010

[THIS PAGE INTENTIONALLY LEFT BLANK]

INSPIRE PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders
of Inspire Pharmaceuticals, Inc.

In our opinion, the financial statements listed in the index appearing under Item 15(a)1 present fairly, in all material respects, the financial position of Inspire Pharmaceuticals, Inc. at December 31, 2009 and December 31, 2008, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2009 in conformity with accounting principles generally accepted in the United States of America. In addition, in our opinion, the financial statement schedule listed in the index appearing under Item 15(a)2 presents fairly, in all material respects, the information set forth therein when read in conjunction with the related financial statements. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2009, based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements and financial statement schedule, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting under Item 9A. Our responsibility is to express opinions on these financial statements, on the financial statement schedule, and on the Company's internal control over financial reporting based on our integrated 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 audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
March 15, 2010

INSPIRE PHARMACEUTICALS, INC.

BALANCE SHEETS
(in thousands, except per share amounts)

	December 31, 2009	December 31, 2008
Assets		
Current assets:		
Cash and cash equivalents	$ 52,256	$ 58,488
Investments	54,367	13,663
Trade receivables, net	22,682	16,544
Prepaid expenses and other receivables	5,479	4,186
Inventories, net	1,717	689
Other assets	153	357
Total current assets	136,654	93,927
Property and equipment, net	4,429	2,925
Assets held-for-sale	402	—
Investments	21,861	200
Restricted deposits	615	615
Intangibles, net	14,748	16,343
Other assets	61	214
Total assets	$ 178,770	$ 114,224
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 10,056	$ 9,843
Accrued expenses	21,246	13,142
Short-term debt and capital leases	19,940	18,430
Total current liabilities	51,242	41,415
Long-term debt and capital leases	5,235	25,175
Other long-term liabilities	3,125	3,247
Total liabilities	59,602	69,837
Commitments and contingencies (Note 14)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 1,860 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value, 100,000 shares authorized; 82,346 and 56,672 shares issued and outstanding, respectively	82	57
Additional paid-in capital	519,462	404,991
Accumulated other comprehensive income/(loss)	68	(193)
Accumulated deficit	(400,444)	(360,468)
Total stockholders' equity	119,168	44,387
Total liabilities and stockholders' equity	$ 178,770	$ 114,224

The accompanying notes are an integral part of these financial statements.

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)

	Year Ended December 31,		
	2009	2008	2007
Revenues:			
Product sales, net	$ 34,961	$ 18,349	$ 3,142
Product co-promotion and royalty	57,198	50,899	45,523
Collaborative research and development	—	1,250	—
Total revenue	92,159	70,498	48,665
Operating expenses:			
Cost of sales	11,271	6,412	1,622
Research and development	51,134	44,637	53,391
Selling and marketing	49,304	54,568	45,543
General and administrative	16,053	14,540	13,986
Restructuring	2,014	—	—
Total operating expenses	129,776	120,157	114,542
Loss from operations	(37,617)	(49,659)	(65,877)
Other income/(expense):			
Interest income	668	2,642	5,082
Interest expense	(3,027)	(4,586)	(2,919)
Loss on investments	—	—	(26)
Other income/(expense), net	(2,359)	(1,944)	2,137
Net loss	$ (39,976)	$ (51,603)	$ (63,740)
Non-cash deemed dividend related to beneficial conversion feature of exchangeable preferred stock	—	—	(8,285)
Net loss attributable to common stockholders	$ (39,976)	$ (51,603)	$ (72,025)
Basic and diluted net loss per common share	$ (0.60)	$ (0.91)	$ (1.61)
Weighted average common shares used in computing basic and diluted net loss per common share	66,797	56,609	44,763

The accompanying notes are an integral part of these financial statements.

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2009	2008	2007
Cash flows from operating activities:			
Net loss	$ (39,976)	$ (51,603)	$ (63,740)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization expense	1,952	2,134	1,781
Depreciation of property and equipment	755	939	891
Asset impairment	484	—	—
Loss/(gain) on disposal of property and equipment	(90)	7	7
Loss on investments	—	—	26
Stock-based compensation expense	5,063	4,443	2,998
Allowance for doubtful accounts	43	(3)	10
Inventory reserve	15	105	125
Changes in operating assets and liabilities:			
Trade receivables	(6,181)	(3,567)	(4,739)
Prepaid expenses and other receivables	(1,413)	345	(765)
Inventories	(1,043)	486	(1,405)
Other assets	—	(40)	—
Accounts payable	(970)	(3,675)	7,221
Accrued expenses and other liabilities	7,860	(671)	5,350
Deferred revenue	—	(371)	371
Net cash used in operating activities	(33,501)	(51,471)	(51,869)
Cash flows from investing activities:			
Purchase of investments	(94,049)	(7,574)	(59,975)
Proceeds from sale of investments	31,945	30,694	74,501
Approval milestone payment	—	—	(19,000)
Restricted cash transfer	—	—	(100)
Purchase of property and equipment	(1,791)	(1,045)	(1,970)
Proceeds from sale of property and equipment	161	—	—
Net cash provided by/(used in) investing activities	(63,734)	22,075	(6,544)
Cash flows from financing activities:			
Proceeds from long-term debt	—	—	40,000
Proceeds from issuance of exchangeable preferred stock, net	—	—	73,605
Proceeds from common stock offering, net	109,000	—	—
Issuance of common stock, net—stock compensation plans	433	88	266
Debt issuance cost	—	—	(100)
Payments on notes payable and capital lease obligations	(18,430)	(14,096)	(3,656)
Net cash provided by/(used in) financing activities	91,003	(14,008)	110,115
Increase/(decrease) in cash and cash equivalents	(6,232)	(43,404)	51,702
Cash and cash equivalents, beginning of year	58,488	101,892	50,190
Cash and cash equivalents, end of year	$ 52,256	$ 58,488	$101,892
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 2,794	$ 4,257	$ 2,255
Supplemental disclosure of non-cash investing information:			
Purchase of equipment included in accounts payable and accrued expenses	$ 1,409	$ —	$ —
Supplemental disclosure of non-cash financing information:			
Conversion of exchangeable preferred stock to common stock	$ —	$ —	$ 73,605

The accompanying notes are an integral part of these financial statements.

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income/(loss)	Accumulated Deficit	Stockholders' Equity
	Number of Shares	Amount				
Balance at December 31, 2006	42,238	$ 42	$323,606	$(152)	$(245,125)	$ 78,371
Issuance of common stock—stock compensation plans	244	1	265	—	—	266
Conversion of Series A Exchangeable Preferred Stock to common stock	14,019	14	73,591	—	—	73,605
Recording of beneficial conversion feature related to the exchange of Series A Exchangeable Preferred Stock	—	—	8,285	—	—	8,285
Accretion of beneficial conversion feature	—	—	(8,285)	—	—	(8,285)
Unrealized gain on investments	—	—	—	193	—	193
Stock-based compensation	—	—	2,998	—	—	2,998
Net loss	—	—	—	—	(63,740)	(63,740)
Balance at December 31, 2007	56,501	57	400,460	41	(308,865)	91,693
Issuance of common stock—stock compensation plans	171	—	88	—	—	88
Unrealized loss on investments	—	—	—	(234)	—	(234)
Stock-based compensation	—	—	4,443	—	—	4,443
Net loss	—	—	—	—	(51,603)	(51,603)
Balance at December 31, 2008	56,672	57	404,991	(193)	(360,468)	44,387
Issuance of common stock—stock compensation plans	118	—	433	—	—	433
Common Stock Offering	25,556	25	108,975	—		109,000
Unrealized gain on investments	—	—	—	261	—	261
Stock-based compensation	—	—	5,063	—	—	5,063
Net loss	—	—	—	—	(39,976)	(39,976)
Balance at December 31, 2009	82,346	$ 82	$519,462	$ 68	$(400,444)	$119,168

The accompanying notes are an integral part of these financial statements.

1. Organization

Inspire Pharmaceuticals, Inc. (the "Company" or "Inspire") was incorporated in October 1993 and commenced operations in March 1995. Inspire is located in Durham, North Carolina, adjacent to the Research Triangle Park.

Inspire has incurred losses and negative cash flows from operations since inception. Based on current operating plans, the Company expects it has sufficient liquidity to continue its planned operations beyond 2010. The Company's liquidity needs will largely be determined by the commercial success of its products and key development and regulatory events. In order to continue its operations substantially beyond 2010 it will need to: (1) successfully increase revenues; (2) obtain additional product candidate approvals; (3) out-license rights to certain of its product candidates; (4) raise additional capital through equity or debt financings or from other sources; (5) reduce spending on one or more research and development programs; and/or (6) further restructure its operations. The Company currently receives revenue from sales of *AzaSite* (azithromycin ophthalmic solution) 1%, its co-promotion of *Elestat* (epinastine HCl ophthalmic solution) 0.05% and royalties on *Restasis* (cyclosporine ophthalmic emulsion) 0.05%. The Company will continue to incur operating losses until revenues reach a level sufficient to support ongoing operations.

2. Summary of Significant Accounting Policies and Concentrations of Risk

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ materially from those estimates.

Cash, Cash Equivalents, Interest and Other Receivables

The Company considers all highly-liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The carrying values of cash, cash equivalents, interest and receivables approximate their fair value due to the short-term nature of these items.

Trade Receivables

The Company's trade receivables consist of co-promotion revenue based on net sales of *Elestat* and royalty revenue based on net sales of *Restasis*, both of which are earned from Allergan, Inc. ("Allergan") and product revenue from sales of *AzaSite*. The Company is required to estimate the amount of trade receivables which ultimately will be uncollectible. The Company calculates an estimate of uncollectible accounts based on a review of specific customer balances, as well as a consideration of other industry and economic environment factors.

Investments

The Company invests in high-credit quality investments in accordance with its investment policy which minimizes the possibility of loss. Per its policy, the Company is able to invest in marketable debt securities that may consist of United States government and government agency obligations, money market and mutual fund investments, municipal and corporate notes and bonds and asset or mortgage-backed securities. The Company's investment policy requires it to purchase high-quality marketable securities with a maximum individual maturity of three years and requires an average portfolio maturity of no more than one year. Investments with original

maturities at date of purchase beyond three months and which mature at or less than 12 months from the balance sheet date are classified as current. Generally, investments with a maturity beyond 12 months from the balance sheet date are classified as long-term. Investments in marketable debt securities are classified as available-for-sale and are carried at fair value with unrealized gains and losses recognized in other comprehensive income (loss). Realized gains and losses are determined using the specific identification method and transactions are recorded on a settlement date basis. Marketable and non-marketable equity investments are evaluated periodically for impairment. If it is determined that a decline of any investment is other than temporary, then the investment would be written down to fair value and the write-down would be included in the Company's operating results.

The Company has an equity investment in Parion Sciences, Inc., a non-public entity for which its fair value is not readily determinable. For this investment in which the Company does not have significant influence and owns less than 5%, the investment is carried at cost and is subject to a write-down for impairment whenever events or changes in circumstances indicate that the carrying value may not be recoverable. As of December 31, 2009 and 2008, this investment's recorded value was $200.

Property and Equipment

Property and equipment is primarily comprised of furniture, software, laboratory and computer equipment which are recorded at cost and depreciated using the straight-line method over their estimated useful lives which range from three to seven years. Leased property and equipment, which includes certain equipment under capital leases, and leasehold improvements are depreciated over the shorter of the lease period or their estimated useful lives.

The carrying values of property and equipment are periodically reviewed to determine if the facts and circumstances suggest that a potential impairment may have occurred. The review includes a determination of the carrying values of assets based on an analysis of undiscounted cash flows over the remaining depreciation period. If the review indicates that carrying values may not be recoverable, the Company will reduce the carrying values to the estimated fair value.

Assets Held-For-Sale

In connection with the restructuring that occurred in the first quarter of 2009, the Company began to market and dispose of its laboratory equipment in the fourth quarter of 2009. The assets held-for-sale are reported at the lower of the carrying value or fair value less costs to sell and the assets are no longer being depreciated. See Note 6 "Restructuring" for additional information. The Company expects to complete the disposal of these assets in 2010. The Company has recorded a net gain of $90 on the disposal of property and equipment for the year ended December 31, 2009.

Restricted Deposits

Restricted deposits consist of cash and cash equivalents which collateralize letters of credit that are required under the terms of certain agreements to which the Company is involved. Restricted deposits are classified as current or long-term based upon the expected release date of such restriction. The carrying amount of these restricted deposits approximates fair value.

Intangible Assets

Costs associated with obtaining patents on the Company's product candidates and license initiation and preservation fees, including milestone payments by the Company to its licensors, are evaluated based on the stage of development of the related product candidate and whether the underlying product candidate has an alternative use. Costs of these types incurred for product candidates not yet approved by the U.S. Food and Drug Administration ("FDA") and for which no alternative future use exists are recorded as expense. In the event a product candidate has been approved by the FDA or an alternative future use exists for a product candidate, patent and license costs are capitalized and amortized over the expected life of the related product candidate. Milestone payments to the Company's collaborators are recognized when the underlying requirement is met.

Upon FDA approval of *AzaSite* in April 2007, the Company paid a $19,000 milestone to InSite Vision Incorporated ("InSite Vision"). The $19,000 is being amortized ratably on a straight-line basis through the term of the underlying patent coverage for *AzaSite*, or March 2019, which represents the expected period of commercial exclusivity. As of December 31, 2009 and 2008, the Company had $4,252 and $2,657, respectively, in accumulated amortization related to this milestone.

The carrying values of intangible assets are periodically reviewed to determine if the facts and circumstances suggest that a potential impairment may have occurred. The review includes a determination of the carrying values of intangible assets based on an analysis of undiscounted cash flows over the remaining amortization period. If the review indicates that carrying values may not be recoverable, the Company will reduce the carrying values to the estimated fair value. The Company had no impairments of its intangible assets for the years ended December 31, 2009, 2008 and 2007.

Other Assets

In December 2006, the Company entered into a loan and security agreement and received an initial loan advance of $20,000. In 2007, the Company amended the loan and security agreement and received additional loan advances totaling $40,000. Expenses associated with entering into the loan agreements, including commitment fees, totaled $1,400 and have been classified as deferred financing costs. At December 31, 2009 and 2008, the Company had $158 and $515, respectively, in deferred financing costs that are being amortized to interest expense over the term of each of the loans, which mature in March 2011, using the effective interest rate method.

Revenue Recognition

The Company records all of its revenue from: (1) sales of *AzaSite;* (2) product co-promotion activities and earned royalties; and (3) collaborative research agreements when realized or realizable and earned. Revenue is realized or realizable and earned when all of the following criteria are met: 1) persuasive evidence of an arrangement exists; 2) delivery has occurred or services have been rendered; 3) the seller's price to the buyer is fixed or determinable; and 4) collectibility is reasonably assured.

Product Revenues

The Company recognizes revenue for sales of *AzaSite* when title and substantially all the risks and rewards of ownership have transferred to the customer, which generally occurs on the date of shipment, with the exception of transactions whereby product stocking incentives were offered approximately one month prior to the product's August 13, 2007 launch. In the United States, the Company sells *AzaSite* to wholesalers and distributors, who, in turn, sell to pharmacies and federal, state and commercial health care organizations.

Sales deductions consist of statutory rebates to state Medicaid, Medicare and other government agencies, contractual rebates with commercial managed care organizations, wholesaler chargebacks, sales discounts (including trade discounts and distribution service fees), allowances for coupon and voucher programs and product returns. These deductions are recorded as reductions to revenue from *AzaSite* in the same period as the related sales with estimates of future utilization derived from historical experience adjusted to reflect known changes in the factors that impact such reserves.

The Company utilizes data from external sources to help it estimate gross-to-net sales adjustments as they relate to the recognition of revenue for *AzaSite* sold. External sourced data includes, but is not limited to, information obtained from certain wholesalers with respect to their inventory levels and sell-through to customers, targeted surveys as well as data from IMS Health, a third-party supplier of market research data to the pharmaceutical industry. The Company also utilizes this data to help estimate and identify prescription trends and patient demand, as well as product levels in the supply chain.

The Company accounts for these sales deductions in accordance with the Financial Accounting Standards Board ("FASB") authoritative guidance on revenue recognition when consideration is given by a vendor to a customer as well as when the right of return exists.

The Company has categorized and described more fully the following significant sales deductions, all of which involve estimates and judgments which the Company considers to be critical accounting estimates, and requires it to use information from external sources.

Rebates and Chargebacks

Statutory rebates to state Medicaid agencies and Medicare and contractual rebates to commercial managed care organizations are based on statutory or negotiated discounts to the selling price. As it can take up to nine months or more for information to be received on actual usage of *AzaSite* in managed care and Medicaid and other governmental programs as well as on the total discounts to be reimbursed, the Company maintains reserves for amounts payable under these programs relating to *AzaSite* sales.

Chargebacks claimed by wholesalers are based on the differentials between product acquisition prices paid by wholesalers and lower government contract pricing paid by eligible customers covered under federally qualified programs.

The amount of the reserve for rebates and chargebacks is based on multiple qualitative and quantitative factors, including the historical and projected utilization levels, historical payment experience, changes in statutory laws and interpretations as well as contractual terms, product pricing (both normal selling prices and statutory or negotiated prices), changes in prescription demand patterns and utilization of our product through private or public benefit plans, and the levels of *AzaSite* inventory in both the wholesale and retail distribution channel. Other factors that the Company may consider, if determined relevant, would include price changes from competitors and introductions of generics and/or competitive new products. The Company acquires prescription utilization data from IMS Health, a third-party supplier of market research data to the pharmaceutical industry. The Company applies these multiple factors, the quantitative historical data along with other qualitative aspects, such as management's judgment regarding future utilization trends, to the respective period's sales of *AzaSite* to determine the rebate accrual and related expense. The Company updates its estimates and assumptions each period and records any necessary adjustments to its reserves. Settlements of rebates and chargebacks typically occur within nine months from point of sale. To the extent actual rebates and chargebacks differ from the

Company's estimates, additional reserves may be required or reserves may need to be reversed, either of which would impact current period product revenue. As of December 31, 2009 and 2008, reserves for rebates and chargebacks were $3,488 and $783, respectively.

Discounts and Other Sales Incentives

Discounts and other sales incentives consist of the following:

- **Prompt pay discounts**—Prompt payment discounts are offered to all wholesalers in return for payment within 30 days following the invoice date. The Company records sales of *AzaSite* net of the discount amount based on historical experience. The Company adjusts the reserve at the end of each reporting period to approximate the percentage discount applicable to the outstanding gross accounts receivable balances.
- **Inventory Management Agreement ("IMA") Fees**—Per contractual agreements with the Company's largest wholesalers (which collectively represented over 85% of 2009 *AzaSite* sales), the Company provides an IMA fee based on a percentage of their purchases of *AzaSite*. The IMA fee rates are set forth in the individual contracts. The Company tracks sales to these wholesalers each period and accrues a liability relating to the unpaid portion of these fees by applying the contractual rates to such sales.
- **Product coupons and vouchers**—Product coupons and vouchers offer patients the ability to receive free or discounted product through their pharmacy or prescribing physician, to whom the Company provides an inventory of coupons or vouchers as applicable. The Company uses a third-party administrator who invoices on a periodic basis for the cost of coupons and vouchers redeemed in the period. The Company bases its estimates on the historical coupon and voucher redemption rate of similar programs.

As of December 31, 2009 and 2008, reserves for discounts and other sales incentives were $889 and $519, respectively.

Product Returns

At the time of sale of *AzaSite*, the Company records product returns allowances based on its estimate of the portion of sales that will be returned by its customers in the future. The return allowances are established in accordance with the Company's return policy. The Company's return goods policy generally allows for returns of *AzaSite* within an 18-month period, from six months prior to the expiration date and up to 12 months following the expiration date, but may differ from customer to customer, depending on certain factors. Future estimated returns of *AzaSite* are based primarily on the return data for comparative products and the Company's own historical experience with *AzaSite*. Historical returns data on *AzaSite* is analyzed on a specific production lot basis. In determining the Company's return allowance, the Company also considers other relevant factors, including:

- Levels of inventory in the distribution channel and any significant changes to these levels
- Estimated expiration date or remaining shelf life of inventory in the distribution channel
- Current and projected demand of *AzaSite* that could be impacted by introductions of generic products and/or introductions of competitive new products; and
- Competitive product recalls and/or discontinuances

The Company's estimates of the level of *AzaSite* inventory in the distribution channel is based on inventory data provided by wholesalers and third-party prescription data. As of December 31, 2009 and 2008, reserves for returns of *AzaSite* were $1,523 and $701, respectively.

Immediately preceding the launch of *AzaSite,* the Company offered wholesalers stocking incentives that allowed for extended payment terms, product discounts, and guaranteed sale provisions (collectively, "special terms"). These special terms were only offered during a specified time period of approximately one month prior to the August 13, 2007 launch of *AzaSite*. Any sales of *AzaSite* made under these special term provisions were accounted for using a consignment model since substantially all the risks and rewards of ownership did not transfer upon shipment. Under the consignment model, the Company did not recognize revenue upon shipment of *AzaSite* purchased with the special terms, but recorded deferred revenue at gross invoice sales price, less all appropriate discounts and rebates, and accounted for *AzaSite* inventory held by the wholesalers as consignment inventory. The Company recognized the revenue from these sales with special terms at the earlier of when the inventory of *AzaSite* held by the wholesalers was sold through to the wholesalers' customers or when such inventory of *AzaSite* was no longer subject to these special terms. At December 31, 2007, the Company had net deferred revenue of $371 related to sales of *AzaSite* considered consignment, which was fully recognized in the three months ended March 31, 2008. All sales subsequent to this specified launch time period include return rights and pricing that are customary in the industry, as discussed above.

Product Co-promotion and Royalty Revenues

The Company recognizes co-promotion revenue based on net sales of *Elestat* and royalty revenue based on net sales of *Restasis*, as defined in the co-promotion agreements, and as reported to Inspire by Allergan. Through the year ended December 31, 2008, the Company actively promoted both *Restasis* and *Elestat* through its commercial organization. As of January 1, 2009, the Company is no longer responsible for the co-promotion of *Restasis*, but the Company continues to receive royalties on Allergan's net sales of *Restasis*. The Company's co-promotion and royalty revenues are based upon Allergan's revenue recognition policy and other accounting policies over which the Company has limited or no control and on the underlying terms of the co-promotion agreements. Allergan recognizes revenue from product sales when goods are shipped and title and risk of loss transfers to the customer. The co-promotion agreements provide for gross sales to be reduced by estimates of sales returns, credits and allowances, normal trade and cash discounts, managed care sales rebates and other allocated costs as defined in the agreements, all of which are determined by Allergan and are outside the Company's control. The Company records a percentage of Allergan's reported net sales to Inspire for *Elestat* and *Restasis,* as co-promotion revenue and royalty revenue, respectively. The Company receives monthly sales information from Allergan and performs analytical reviews and trend analyses using prescription information that it receives from IMS Health. In addition, the Company exercises its audit rights under the contractual agreements with Allergan to annually perform an examination of Allergan's sales records of both *Restasis* and *Elestat*. The Company makes no adjustments to the amounts reported to it by Allergan other than reductions in net sales to reflect the incentive programs managed by the Company. The Company offers and manages certain incentive programs associated with *Elestat,* which are utilized by it in addition to those programs managed by Allergan. The Company reduces co-promotion revenue from net sales of *Elestat* by estimating the portion of sales that are subject to these incentive programs based on information reported to it by a third-party administrator of the incentive program. The rebates associated with the programs that the Company manages represent an insignificant amount, as compared to the rebate and discount programs administered by Allergan and as compared to the Company's aggregate co-promotion and royalty revenue. Under the co-promotion agreement for *Elestat*, the Company is obligated to meet predetermined minimum calendar year net sales target levels. If the annual minimum is not achieved, the Company records revenues using a reduced percentage of net

sales based upon its level of achievement of the predetermined calendar year net sales target levels. Amounts receivable from Allergan in excess of recorded co-promotion revenue are recorded as deferred revenue. Calendar year 2009 was the last year in which there is a minimum annual net sales target level for *Elestat* under the co-promotion agreement.

Collaborative Research and Development Revenues

The Company recognizes revenue under its collaborative research and development agreements when it has performed services under such agreements or when the Company or its collaborative partner have met a contractual milestone triggering a payment to the Company. The Company recognizes revenue from its research and development service agreements ratably over the estimated service period as related research and development costs are incurred and the services are substantially performed. Upfront non-refundable fees and milestone payments received at the initiation of collaborative agreements for which the Company has an ongoing research and development commitment are deferred and recognized ratably over the period in which the services are substantially performed. This period, if not defined in the collaborative agreement, is based on estimates by the Company's management and the progress towards agreed upon development events as set forth in the collaborative agreements. These estimates are subject to revision as the Company's development efforts progress and it gains knowledge regarding required additional development. Revisions in the commitment period are made in the period that the facts related to the change first become known. If the estimated service period is subsequently modified, the period over which the upfront fee or revenue related to ongoing research and development services is modified on a prospective basis. The Company is also entitled to receive milestone payments under its collaborative research and development agreements based upon the achievement of agreed upon development events that are substantively at-risk by its collaborative partners or the Company. This collaborative research and development revenue is recognized upon the achievement and acknowledgement of the Company's collaborative partner of a development event, which is generally at the date payment is received from the collaborative partner or is reasonably assured. Accordingly, the Company's revenue recognized under its collaborative research and development agreements may fluctuate significantly from period to period.

Research and Development

Research and development expenses include all direct costs and indirect development costs related to the development of the Company's portfolio of product candidates. These expenses include: salaries for research and development personnel, consulting fees, clinical trial costs, including the development and manufacture of drug product for clinical trials, sponsored research costs, clinical trial insurance, up-front license fees, milestone and royalty payments relating to research and development, and other fees and costs related to the development of product candidates. These costs have been charged to operating expense as incurred. License milestone payments to the Company's licensors are recognized as expense when the underlying requirement is met or service has been provided.

Income Taxes

The Company accounts for income taxes using the liability method which requires the recognition of deferred tax assets or liabilities for the temporary differences between financial reporting and tax bases of the Company's assets and liabilities and for tax carryforwards at enacted statutory tax rates in effect for the years in which the differences are expected to reverse. The effect on deferred taxes of a change in tax rates is recognized

in income in the period that includes the enactment date. The Company accounts for uncertain tax positions in accordance with FASB authoritative guidance regarding the accounting for taxes. Significant management judgment is required in determining the provision for income taxes, deferred tax assets and liabilities and any valuation allowance recorded against net deferred tax assets. The Company has recorded a valuation allowance against all potential tax assets due to uncertainties in the Company's ability to utilize the deferred tax assets, primarily consisting of certain net operating losses carried forward, before they expire. The valuation allowance is based on estimates of taxable income in each of the jurisdictions in which the Company operates and the period over which the deferred tax assets will be recoverable.

Stock-Based Compensation

The Company recognizes stock-based compensation expense in accordance with FASB authoritative guidance regarding the accounting for share-based payments, which requires that share-based payments be measured at fair value and recognized as compensation expense over the service period in which the awards are expected to vest. The Company utilizes the Black-Scholes option-pricing model to value its share-based awards and recognizes compensation expense on a straight-line basis over the vesting periods of the awards, which is generally three to five years. The Company considers many factors when estimating expected forfeitures, including types of awards, employee class, and historical experience. Expected volatility is determined based on the Company's own historical volatility. The estimation of share-based awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from the Company's current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. Significant management judgment is required in determining estimates of future stock price volatility, forfeitures and expected life to be used in the valuation of the awards. Actual results, and future changes in estimates, may differ substantially from current estimates.

In accordance with SEC authoritative guidance, if a company concludes that its historical share option experience does not provide a reasonable basis upon which to estimate expected term, it may use the simplified method to estimate the expected term of its options. The Company has utilized the simplified method to estimate expected term for share-based payment awards issued in the years ended December 31, 2009, 2008 and 2007. See Note 11 to the Financial Statements for a further discussion on stock-based compensation.

Net Loss Per Common Share

Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding and dilutive potential common shares then outstanding. Dilutive potential common shares consist of shares issuable upon the exercise of stock options and restricted stock units that are paid in shares of the Company's stock upon conversion. The calculation of diluted earnings per share for the years ended December 31, 2009, 2008 and 2007 does not include 261, 183 and 457, respectively, of potential common shares, as their impact would be antidilutive.

Comprehensive Loss

Accumulated other comprehensive loss is comprised of unrealized gains and losses on marketable securities and is disclosed as a component of stockholders' equity. At December 31, 2009, the Company had $68 of unrealized gains on its investments. At December 31, 2008, the Company had $193 of unrealized losses on its investments.

(in thousands, except per share amounts)

Comprehensive loss consists of the following components for the years ended December 31,:

	2009	2008	2007
Net loss	$(39,976)	$(51,603)	$(63,740)
Adjustment for realized losses in net loss	—	—	26
Change in unrealized gain/(losses) on investments	261	(234)	167
Total comprehensive loss	$(39,715)	$(51,837)	$(63,547)

Advertising

The Company engages in general and direct-response advertising when promoting and marketing *AzaSite* and *Elestat*. These advertising costs are expensed as the costs are incurred. Advertising and product promotion expenses were $9,666, $12,314 and $11,541 for the years ended December 31, 2009, 2008 and 2007, respectively.

Significant Customers and Risk

The Company relies primarily on three pharmaceutical wholesalers to purchase and supply the majority of *AzaSite* at the retail level. These three pharmaceutical wholesalers accounted for greater than 85% of all *AzaSite* product sales in the years ended December 31, 2009 and 2008, respectively, and account for 27% of the Company's outstanding trade receivables as of December 31, 2009. The loss of one or more of these wholesalers as a customer could negatively impact the commercialization of *AzaSite*. All co-promotion and royalty revenues recognized and recorded were from one collaborative partner, Allergan. The Company is entitled to receive co-promotion revenue from net sales of *Elestat* and royalty revenue from net sales of *Restasis* under the terms of its collaborative agreements with Allergan, and accordingly, all trade receivables for these two products are solely due from Allergan and account for 72% of the Company's outstanding trade receivables as of December 31, 2009. Due to the nature of these agreements, Allergan has significant influence over the commercial success of *Restasis* and *Elestat*.

Risk from Generic Competition

The Company's revenues are subject to risk due to generic product entrants. The *Elestat* co-promotion agreement provides that unless earlier terminated, the term of such agreement will be in effect until the earlier of (i) the approval and launch of the first generic epinastine product after expiration of the FDA exclusivity period covering *Elestat* in the United States, or (ii) the approval and launch of the first over-the-counter epinastine product after expiration of the listing of *Elestat* in the FDA's Orange Book. Following the termination of such co-promotion agreement, the Company will no longer have rights to co-promote *Elestat*. The Company will be entitled to receive post-termination payments from Allergan, based on any remaining net sales of *Elestat* for a period of 36 months. The Company has been notified that Boehringer Ingelheim and Allergan received notices from four companies, advising that each company filed an Abbreviated New Drug Application ("ANDA") for a generic version of *Elestat*. The date of submission of the first ANDA filing to the FDA Office of Generic Drugs was October 14, 2008. The Company does not know when the FDA will complete its review of these ANDAs, but it expects that a generic form of epinastine could be launched in the second half of 2010.

Following the expiration of a use patent in August 2009, the manufacture and sale of *Restasis* is protected in the United States by a formulation patent that expires in May 2014. While a formulation patent may afford certain limited protection, a competitor may attempt to gain FDA approval for a cyclosporine product using a

different formulation. Furthermore, following the expiration of the formulation patent in 2014, a generic form of *Restasis* could be introduced into the market. If and when *Restasis* experiences competition from a cyclosporine product, including a generic cyclosporine product, the Company's revenues attributable to *Restasis* may be significantly impacted.

Credit Risk

Cash equivalents and investments are financial instruments which potentially subject the Company to concentration of risk to the extent recorded on the balance sheet. The Company deposits excess cash with major financial institutions in the United States. Balances may exceed the amount of insurance provided on such deposits. Management of the Company believes it has established guidelines for investment of its excess cash relative to diversification and maturities that maintain safety and liquidity. To minimize the exposure due to adverse shifts in interest rates, the Company currently maintains a portfolio of investments with an average maturity of 12 months or less as of December 31, 2009.

Risks from Third Party Manufacturing and Distribution Concentration

The Company relies on single source manufacturers for its commercial products and product candidates. Allergan is responsible for the manufacturing of both *Restasis* and *Elestat* and relies on single source manufacturers for the active pharmaceutical ingredients in both products. The Company relies on InSite Vision for the supply of the active pharmaceutical ingredient for *AzaSite*, which InSite Vision obtains from a single source manufacturer. The Company is responsible for the remaining finished product manufacturing of *AzaSite*, for which it relies on a single source manufacturer. Additionally, the Company relies upon a single third party to provide distribution services for *AzaSite*.

The Company relies upon one vendor as the sole manufacturer of the supply of active pharmaceutical ingredients for both *Prolacria* and denufosol; however, the Company has initiated development of a secondary supplier for denufosol.

Effective September 25, 2009, the Company and Yamasa Corporation entered into a Technology License Agreement for the Manufacture of Denufosol. The purpose of the agreement is to facilitate the transfer of the current denufosol manufacturing technology, including intellectual property, to an additional manufacturer and thus enable a two-supplier strategy for denufosol. In consideration of the grant of rights under the agreement, in October 2009, the Company paid Yamasa three hundred million Japanese Yen (¥ 300,000,000), which was approximately $3,302 at the prevailing exchange rate. Additionally, the Company shall pay Yamasa (i) three hundred million Yen (¥ 300,000,000) within thirty (30) days after the receipt of a process validation report by December 31, 2010 following the successful completion of three validation batches; and (ii) four hundred million Yen (¥ 400,000,000) within thirty (30) days after both (a) the acceptance of a pre-approval inspection of denufosol at Yamasa by the FDA, and (b) the approval of a New Drug Application of a formulated denufosol drug product at Inspire by the FDA.

Delays in the manufacture or distribution of any product or manufacture of any product candidate could adversely impact the marketing of the Company's products or the development of the Company's product candidates. Furthermore, the Company has no control over the manufacturing or the overall product supply chain of *Restasis* and *Elestat*.

Recent Accounting Pronouncements

In January 2010, the FASB issued authoritative guidance for improving disclosures about fair value measurements. This guidance requires some new disclosures and clarifies some existing disclosure requirements about fair value measurement. The new disclosure requirements are effective for interim and annual reporting periods beginning after December 15, 2009, except for the disclosures about purchases, sales, issuances, and settlements in the roll forward of activity in Level 3 fair value measurements. Those disclosures are effective for fiscal years beginning after December 15, 2010, and for interim periods within those fiscal years. Since the new guidance only impacts financial statement disclosures, there will be no impact to the Company's financial position or results of operations upon adoption.

In October 2009, the FASB issued authoritative guidance regarding revenue arrangements with multiple deliverables. The guidance requires entities to allocate revenue in an arrangement using estimated selling prices of the delivered goods and services based on a selling price hierarchy. The guidance further eliminates the residual method of revenue allocation and requires revenue to be allocated using the relative selling price method. The new guidance should be applied on a prospective basis for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010, with early adoption permitted. The Company is currently assessing the impact of adopting this new guidance.

In August 2009, the FASB issued authoritative guidance regarding measuring liabilities at fair value. The authoritative guidance sets forth the types of valuation techniques to be used to value a liability when a quoted price in an active market for the identical liability is not available. It also clarifies transfer restrictions on the fair value of a liability and the ability to use the fair value of a liability that is traded as an asset as an input to the valuation of the underlying liability. The authoritative guidance is effective for interim and annual periods beginning after August 26, 2009. The Company has assessed the impact of this new guidance and expects no material impact to its financial statements upon adoption.

In May 2009, the FASB issued authoritative guidance regarding subsequent events. The authoritative guidance establishes general standards of accounting for and disclosure of events that occur after the balance sheet date but before financial statements are issued or are available to be issued. The authoritative guidance is effective for interim and annual periods ending after June 15, 2009.

In April 2009, the FASB issued authoritative guidance to aid in determining fair value when the volume and level of activity for the assets or liabilities have significantly decreased and when identifying transactions are not orderly, such as a forced liquidation or distressed sale. The authoritative guidance became effective for the Company on April 1, 2009, and the adoption of the guidance did not have a material impact on the Company's consolidated financial statements.

In April 2009, the FASB issued authoritative guidance on the recognition and presentation of other-than-temporary impairments. The authoritative guidance incorporates impairment guidance for debt securities from various sources of authoritative literature and clarifies the interaction of the factors that should be considered when determining whether a debt security is other than temporarily impaired. The authoritative guidance became effective for the Company on April 1, 2009 and the adoption of the guidance did not have a material impact on the Company's consolidated financial statements.

In April 2009, the FASB issued authoritative guidance to require disclosures about fair value of financial instruments in interim financial statements as well as in annual financial statements. The authoritative guidance is effective for interim periods ending after June 15, 2009, and the Company has adopted the guidance and has provided the additional disclosures as required.

(in thousands, except per share amounts)

3. Fair Value

The Company's financial assets recorded at fair value on a recurring basis have been categorized based upon a fair value hierarchy in accordance with FASB authoritative guidance. Under the guidance, fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (the "exit price") in an orderly transaction between market participants at the measurement date. The guidance establishes a hierarchy for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's own assumptions about the market participant assumptions that would be used in pricing the asset or liability based on the best information available in the circumstances. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (level 1 measurements) and the lowest priority to unobservable inputs (level 3 measurements). As of January 1, 2009, the Company adopted the guidance for its fair value measure of non-financial assets and liabilities and there was no material impact.

The Company has not elected the fair value option for financial assets and liabilities existing at January 1, 2008 that were not already measured at fair value or newly transacted in the years ended December 31, 2009 and 2008. Any future transacted financial assets or liabilities will be evaluated for the fair value election.

The following fair value hierarchy tables present information about the Company's financial assets measured at fair value on a recurring basis as of December 31, 2009 and 2008:

	Total Balance	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)
As of December 31, 2009:			
Cash equivalents	$ 41,052	$36,053	$ 4,999
Investments—Available-for-sale securities:			
U.S. Treasury	5,980	5,980	—
U.S. Government agencies	12,658	—	12,658
Corporate bonds and commercial paper	44,778	—	44,778
Negotiated certificates of deposit	12,612	—	12,612
Total	$117,080	$42,033	$75,047
As of December 31, 2008:			
Cash equivalents	$ 53,062	$51,066	$ 1,996
Investments—Available-for-sale securities:			
U.S. Treasury	5,000	5,000	—
Corporate bonds and commercial paper	8,663	—	8,663
Total	$ 66,725	$56,066	$10,659

Level 1 fair value measurements are based on quoted market prices in active markets and include U.S. government and agency securities. Level 1 cash equivalents consist of investments concentrated in money market funds which are primarily invested in U.S. Treasury securities.

Level 2 fair value measurements are based on quoted prices in markets that are not active, broker dealer quotations, or other methods by which all significant inputs are observable, either directly or indirectly. Level 2 cash equivalents and available-for-sale securities consist of investments in corporate bonds and commercial paper, U.S. government agencies and negotiated certificates of deposit.

(in thousands, except per share amounts)

The Company's investment policy dictates that investments in money market instruments are limited to those that have a rating of at least A-1 and P-1 according to Standard & Poor's and Moody's Investor Services, respectively. Likewise, for investments made in corporate obligations, the Company's investment policy requires ratings of at least A and A-2 according to Standard & Poor's and Moody's Investor Services. The Company does not have any direct investments in auction-rate securities or securities that are collateralized by assets that include mortgages or subprime debt.

Non-recurring fair value amounts for assets held at December 31, 2009 were $402 and are considered Level 3. These assets represent assets held-for-sale and reflect the lower of the carrying value or fair value less costs to sell. As a result of its restructuring activity, the Company assessed the fair value of assets, primarily property and equipment associated with idle lab facilities, on a non-recurring basis. In the first quarter of 2009, the Company recorded an impairment of $484 to reflect the estimated fair value of the idle assets, based on internally established estimates and the selling prices of similar assets. In the fourth quarter of 2009, the Company began marketing and disposing of all its laboratory equipment. Fair value of this equipment was assessed by the third-party marketer and no additional impairment charges were recorded.

4. Investments

A summary of the fair market value of the Company's investments by classification, as well as contractual maturities of marketable debt securities, is as follows:

	December 31,	
	2009	2008
Available-for-sale debt securities:		
Less than one year	$54,367	$13,663
After one year through five years	21,661	—
Total available-for-sale debt securities	$76,028	$13,663
Preferred stock	200	200
Total Investments	$76,228	$13,863

The following is a summary of the Company's marketable debt securities which are classified as available-for-sale as of December 31, 2009 and 2008:

	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
As of December 31, 2009:				
Corporate bonds and commercial paper	$44,702	$ 88	$ (12)	$44,778
U.S. Treasury	5,981		(1)	5,980
U.S. Government agencies	12,664	—	(6)	12,658
Negotiated certificates of deposit	12,612	—	—	12,612
Total	$75,959	$ 88	$ (19)	$76,028
As of December 31, 2008:				
Corporate bonds and commercial paper	$ 8,858	$ 5	$(200)	$ 8,663
U.S. Treasury	4,998	2	—	5,000
Total	$13,856	$ 7	$(200)	$13,663

(in thousands, except per share amounts)

The Company does not consider its investment in available-for-sale debt securities to be other-than-temporarily impaired at December 31, 2009.

The following table shows the gross unrealized losses and fair value of the Company's investment in marketable debt securities with unrealized losses that are deemed to be temporarily impaired, aggregated by length of time that the individual securities have been in a continuous unrealized loss position as of December 31, 2009 and 2008:

	Less than 12 months	
	Fair Value	Unrealized Loss
As of December 31, 2009:		
Corporate bonds	$20,586	$ (12)
U.S. Treasury	5,980	(1)
U.S. Government agencies	9,158	(6)
Total	$35,724	$ (19)
As of December 31, 2008:		
Corporate bonds	$ 6,140	$(200)
Total	$ 6,140	$(200)

The unrealized losses on the Company's investments in corporate bonds as of December 31, 2009 were primarily due to changes in credit ratings and changes in market interest rates. The unrealized losses on the Company's investments in corporate bonds as of December 31, 2008 were primarily due to changes in credit ratings. The contractual terms of these investments do not permit the issuer to settle the securities at a price less than the amortized cost of the investment. Because the Company has the ability and intent to hold its investments until a recovery of fair value, which may be at maturity, the Company does not consider its investments to be other-than-temporarily impaired at December 31, 2009. The Company did not have any investments in marketable debt securities that have been in a continuous unrealized loss position for 12 months or greater as of December 31, 2009 and 2008. Gross realized losses on the Company's available-for-sale securities were $26 for the year ended December 31, 2007. There were no realized gains or losses on the Company's available-for-sale securities for the years ended December 31, 2009 and 2008.

5. Inventories

The Company's inventories are related to *AzaSite* and are valued at the lower of cost or market using the first-in, first-out (i.e., FIFO) method. Cost includes materials, labor, overhead, shipping and handling costs. The Company's inventories are subject to expiration dating and the Company has reserved for potential overstocking. The Company's inventories consisted of the following:

	As of	
	December 31, 2009	December 31, 2008
Finished Goods	$ 808	$ 47
Work-in-Process	96	160
Raw Materials	838	492
Total Inventories	$1,742	$699
Less Valuation Reserve	(25)	(10)
Total Inventories, net	$1,717	$689

(in thousands, except per share amounts)

During the years ended December 31, 2009, 2008 and 2007, the Company recorded valuation reserves of $15, $105 and $125, respectively, for potential overstocking and short-dated product. During the year ended December 31, 2008, the Company wrote-off approximately $220 of short-dated product from finished goods.

6. Restructuring

In March 2009, the Company announced that it had restructured its operations during the first quarter of 2009, eliminating preclinical and drug discovery activities and refocusing its resources on the development of existing later-stage clinical programs and commercially available products. In connection with the restructuring, the Company recorded restructuring charges of $2,014 for the year ended December 31, 2009, which are reported as a separate line item in the accompanying Condensed Statement of Operations. The Company recorded its restructuring activities in accordance with FASB authoritative guidance regarding the accounting for the impairment and disposal of long-lived assets and the accounting for costs associated with exit or disposal activities.

The following table summarizes the components of the restructuring charges:

	Year ended December 31, 2009		
	Accruals	Non-cash items	Total
Facilities related	$ 255	$—	$ 255
Employee separation costs	1,072	—	1,072
Asset impairment	—	484	484
Contracts	203	—	203
Total Restructuring Charges	$1,530	$484	$2,014

Employee separation costs consist of one-time termination benefits, primarily severance costs, associated with the reduction in the Company's workforce.

Asset impairments consist of property and equipment, primarily lab equipment, that was used for discovery and preclinical research activities at the Company's facility. The Company performed an impairment analysis and determined that the carrying value of the idle assets exceeded their fair value and recorded an impairment charge of $484. Fair value was based on internally established estimates and the selling prices of similar assets.

Contract charges consist of costs associated with contractual commitments and work performed subsequent to the restructuring related to programs the Company no longer supports as part of its planned ongoing research and development activities.

Facility related charges consist of estimated losses associated with leased lab space at the Company's Durham, North Carolina headquarters that the Company no longer uses in its operations. The unoccupied leased space is approximately 14,000 square feet and the lease term is through January 2011. The Company used a discounted cash-flow analysis to calculate the amount of this liability. The probability-weighted discounted cash-flow analysis is based on management's assumptions and estimates of its ongoing lease obligations, including contractual rental commitments, build-out commitments and building operating costs, estimates of income from subleases, and market conditions for similar rental properties in its geographic area. The estimated cash flows were discounted using a credit-adjusted risk free rate of approximately 15%. The Company expects to incur approximately $45 of accretion expense over the term of the lease.

(in thousands, except per share amounts)

The following table sets forth activity in the restructuring liability for the year ended December 31, 2009:

	Employee separation costs	Facilities related charges	Other restructuring charges	Total
Balance at December 31, 2008	$ —	$ —	$ —	$ —
Accruals	1,072	255	203	1,530
Payments	(1,072)	(140)	(203)	(1,415)
Balance at December 31, 2009	$ —	$ 115	$ —	$ 115

The liability associated with employee separation costs was fully paid as of December 31, 2009. The liability associated with facilities will be reduced as monthly rental payments are made through the lease term, which ends in January 2011.

7. Property and Equipment

Property and equipment consist of the following:

	Useful Life (Years)	December 31,	
		2009	2008
Equipment	5	$ 6,339	$ 6,228
Leasehold improvements	Lesser of lease term or 5 years	2,236	2,225
Software	5	1,165	1,134
Furniture and fixtures	7	836	983
Computer hardware	3	578	979
		11,154	11,549
Less accumulated depreciation		(6,725)	(8,624)
Property and equipment, net		$ 4,429	$ 2,925

8. Accrued Expenses

Accrued expenses are comprised of the following:

	December 31,	
	2009	2008
Compensation and benefits	$ 7,574	$ 6,060
Allowances for discounts, rebates, chargebacks and returns	5,900	2,004
Development costs	4,617	3,226
Selling and marketing costs	906	479
Inventory	893	—
Professional fees	314	351
Duties and taxes	226	168
Accrued interest	169	293
Other	647	561
	$21,246	$13,142

The carrying value of accrued expenses approximates fair value due to their short-term settlement.

(in thousands, except per share amounts)

9. Debt

In December 2006, the Company entered into a loan and security agreement with two participating financial institutions, which provided a term loan facility to the Company in an aggregate amount of $40,000. Any borrowings under the loan agreement are collateralized by substantially all of the Company's assets, with the exception of its intellectual property but including all accounts, license and royalty fees and other revenues and proceeds arising from its intellectual property. In addition, the Company established and maintains its primary depository accounts and security accounts with one of the participating financial institutions and will keep a certain percentage of its cash and investments within these accounts depending upon its total cash and investment balances. In June 2007, the Company amended the loan and security agreement with the two participating financial institutions to enable the Company to draw upon a new supplemental term loan facility in the amount $20,000, effectively increasing the total term loan facility to $60,000. The Company has borrowed the full $60,000 available under the term loan facility. The interest rates associated with each of the borrowings under the facility range from approximately 7.6% to 8.0%.

The final maturity date for all loan advances under the original term loan facility and the supplemental term loan facility is March 2011. Interest accrues on the unpaid principal amount of each loan advance at a per annum rate equal to the five-year U.S. Treasury note yield plus a predetermined percentage at the time each advance is made. Repayment of each advance is made according to a schedule of six monthly installments of interest-only followed by equal monthly installments of principal and interest until the maturity date. During the term of the loan and security agreement, the Company is required to maintain minimum liquidity levels at a ratio of 1:1.35 based on the balance of the outstanding advances of the first $40,000 under the original term loan facility. There is no minimum liquidity requirement on the $20,000 borrowed under the supplemental term loan facility. In addition to other financial and non-financial covenants within the agreement, the agreement contains a subjective acceleration clause such that repayment could be accelerated upon a material adverse change to the business, properties, assets, financial condition or results of operations of the Company. In addition, under the terms of the agreement, the Company may not enter into certain transactions such as a merger, acquisition, additional indebtedness or dispose of certain assets of the business as defined in the agreement without written approval of the lenders. The Company has the right to prepay the principal of any advance in minimum incremental amounts of $1,000. Any prepayment of borrowings made under the original term loan facility are not subject to a penalty; however, any prepayments of borrowings made under the new supplemental term loan facility are subject to a 2% penalty, if prepaid within the first two years. All repayments of principal by the Company are subject to a final payment of $1,200, equal to 2% of the principal amount being repaid. Amounts cannot be re-borrowed by the Company once repaid. At December 31, 2009, the Company was in compliance with all of the covenants under the loan and security agreement and projects that it will be throughout 2010.

As of December 31, 2009, the Company had net borrowings of $25,175 under the loan and security agreement that bears interest at a weighted average rate of 7.8%. The fair value of the Company's long-term debt as of December 31, 2009 is $24,366. The fair value is estimated by discounting the projected cash flows using the current rates available to the Company as of the balance sheet date for debt of similar terms and maturities. Scheduled maturities, representing principal repayments, of the term loan facility are as follows:

Term-Loan Maturities	
2010	$19,940
2011	5,235
Total	$25,175

10. Stockholders' Equity

Sales of Common Stock

In August 2009, the Company completed a public offering of 25,556 shares of its common stock at a price of $4.50 per share, which included the underwriter's over-allotment allocation of an additional 3,333 shares, for gross proceeds of $115,000. Net proceeds were $109,000, after deducting underwriting discounts and offering expenses, including reimbursing Warburg Pincus Private Equity IX, L.P. ("Warburg"), a related party, for $500 of expenses incurred. Warburg purchased $40,000, or 8,889 shares, of the common stock offering for total holdings of 22,907 shares of the Company's common stock, which represented approximately 28% of the Company's outstanding stock as of December 31, 2009.

The sale of the shares was made pursuant to the Company's registration statement on Form S-3 filed with the SEC on March 9, 2007, which provided the Company the ability to offer for sale approximately $130,000 of securities, including common stock, preferred stock, debt securities, depositary shares and securities warrants.

In July 2007, the Company sold approximately 140 shares of its Series A Exchangeable Preferred Stock, par value $0.001 per share (the "Exchangeable Preferred Stock"), to Warburg at a price per share of $535.00, for aggregate gross proceeds of $75,000 under a Securities Purchase Agreement. The purchase price was based on a $5.35 per share value for the Company's common stock, par value $0.001 per share. The Company incurred issuance costs of approximately $1,395 in connection with the sale of the Exchangeable Preferred Stock. The Exchangeable Preferred Stock was exchangeable for shares of common stock at a ratio of 1:100. In October 2007, the Company held a special meeting of stockholders at which the proposed exchange of all outstanding Exchangeable Preferred Stock for shares of the Company's common stock was approved by the Company's stockholders. The total number of shares of common stock issued in the exchange was 14,019. Subsequent to the exchange, the Company retired the 140 shares of the Exchangeable Preferred Stock, reducing total authorized shares of preferred stock available for issuance to 1,860.

The Exchangeable Preferred Stock was accounted for in accordance with FASB authoritative guidance on accounting for convertible securities with beneficial conversion features. The difference between the effective conversion price per share of underlying common stock in the exchange provision and the market value per share of common stock as of the closing date of the Exchangeable Preferred Stock transaction resulted in the recording of an embedded contingent beneficial conversion feature, which is required to be treated as a non-cash deemed dividend to preferred stockholders. Upon the stockholders' approval on October 31, 2007, the contingency was resolved and the Exchangeable Preferred Stock was immediately converted to common stock, resulting in full accretion of the beneficial conversion feature. The calculated value of the beneficial conversion feature was approximately $8,285 and was credited to additional paid-in capital upon resolution of the contingency in the quarter ended December 31, 2007. Due to the absence of retained earnings, the accretion of the beneficial conversion feature was recorded as a debit to additional paid-in-capital.

The holders of the Company's common stock are entitled to receive dividends from time to time as may be declared by the Board of Directors, but a common stock dividend has never been declared, nor is a dividend payment expected in the near-term. The holders of shares of common stock are entitled to one vote for each share held with respect to all matters voted on by the stockholders of the Company.

Rights Agreement

In October 2002, the Company entered into a Rights Agreement with Computershare Trust Company. The Rights Agreement provides for a dividend of one preferred stock purchase right for each outstanding share of the

(in thousands, except per share amounts)

Company's common stock. Each right entitles a stockholder, after the rights become exercisable, to buy 1/1,000th of a share of Inspire's Series H Preferred Stock at an exercise price of $50. Each right will become exercisable following the tenth day after an acquiring person or group acquires, or announces its intention to acquire, 15% or more of the common stock. The Company will be entitled to redeem the rights at $0.001 per right at any time on or before the close of business on the tenth day following acquisition by a person or group of 15% or more of the common stock. Under the Rights Agreement, if a person acquires 15% or more of the common stock without the approval of the Company's Board of Directors, all other stockholders will have the right to purchase securities from the Company at a price that is less than its fair market value, which would substantially reduce the value of the common stock owned by the acquiring person. As a result, the rights will cause substantial dilution to a person or group that attempts to acquire the Company on terms not approved by the Company's Board of Directors, except pursuant to an offer conditioned on a substantial number of Rights being acquired. The rights should not interfere with any merger or other business combination approved by the Board of Directors since the rights may be redeemed by the Company at the redemption price of $0.001 prior to the occurrence of a distribution date. In connection with the transaction with Warburg, the Company and Computershare entered into a First Amendment to Rights Agreement dated July 17, 2007. The First Amendment to Rights Agreement provides that Warburg and its affiliates will be exempt from the definition of an "Acquiring Person" under the Rights Agreement, unless Warburg or certain of its affiliates becomes the beneficial owner of the lesser of: (x) 32.5% of the Company's voting securities on a fully diluted basis and (y) 34.9% of the Company's then outstanding voting securities plus the outstanding Exchangeable Preferred Stock on an as exchanged to common stock basis.

11. Stock-Based Compensation

The Company accounts for stock-based compensation in accordance with FASB authoritative guidance regarding share-based payments. Total stock-based compensation was allocated as follows:

	Year Ended December 31,		
	2009	2008	2007
Research and development	$1,295	$1,319	$ 822
Selling and marketing	1,849	1,402	882
General and administrative	1,919	1,722	1,294
Total stock-based compensation expense	$5,063	$4,443	$2,998

Equity Compensation Plans

The Company has two stock-based compensation plans, the Amended and Restated 1995 Stock Plan (the "1995 Plan") and the Amended and Restated 2005 Equity Compensation Plan (the "2005 Plan"), that allow for share-based payments to be granted to directors, officers, employees and consultants. The 1995 Plan allows for the granting of non-qualified stock options and restricted stock to directors, officers, employees and consultants. The 2005 Plan allows for the granting of both incentive and non-qualified stock options, stock appreciation rights, restricted stock and restricted stock units to directors, officers, employees and consultants. At December 31, 2009, there were 389 and 896 shares available for grant as options or other forms of share-based payments under the 1995 Plan and 2005 Plan, respectively.

The Board of Directors, or an appropriate committee of the Board of Directors, determines the terms of all options and other equity arrangements under both plans. The maximum term for any option grant under the 1995 Plan and the 2005 Plan are ten and seven years, respectively, from the date of the grant. Prior to July 2006,

(in thousands, except per share amounts)

options granted to employees under both plans generally vested 25% upon completion of one full year of employment from date of grant and on a monthly basis over the following three years of their employment and the term of the options was the maximum permitted under the applicable plan. Beginning in July 2006, the Compensation Committee of the Company's Board of Directors authorized stock option grants with a three-year vesting period and a term of five years for all future issuances to non-executive employees. Under these new terms, options granted to non-executive employees will vest 33% upon completion of one full year of employment from date of grant and on a monthly basis over the following two years of their employment. The vesting period typically begins on the date of hire for new employees and on the date of grant for existing employees.

Basis for Fair Value Estimate of Share-Based Payments

Stock Options

The Company uses its own historical volatility to estimate its future volatility. Actual volatility, and future changes in estimated volatility, may differ substantially from the Company's current estimates.

The Company utilizes the simplified method of calculating the expected life of options for grants made to its employees under the 1995 Plan and 2005 Plan in accordance with authoritative guidance due to the lack of adequate historical data with regard to exercise activity on options. For options granted to directors under the 1995 Plan or the 2005 Plan, the Company uses the contractual term of seven years as the expected life of options. The Company will continue with these assumptions in determining the expected life of options under the 1995 Plan and the 2005 Plan until such time that adequate historical data is available. The Company estimates the forfeiture rate based on its historical experience. These estimates will be revised in future periods if actual forfeitures differ from the estimate. Changes in forfeiture estimates impact compensation cost in the period in which the change in estimate occurs.

The table below presents the weighted average expected life in years of options granted under the two plans as described above. The risk-free rate of the stock options is based on the U.S. Treasury yield curve in effect at the time of grant, which corresponds with the expected term of the option granted. The fair value of share-based payments, granted during the period indicated, was estimated using the Black-Scholes option pricing model with the following assumptions and weighted average fair values as follows:

	Stock Options for Year Ended December 31,		
	2009	2008	2007
Risk-free interest rate	1.73%	2.43%	4.43%
Dividend yield	0%	0%	0%
Expected volatility	71%	65%	67%
Expected life of options	3.9 years	3.9 years	3.9 years
Weighted average fair value of grants (per option)	$ 2.34	$ 2.01	$ 3.22

(in thousands, except per share amounts)

The following table summarizes the stock option activity for both the 1995 Plan and 2005 Plan:

	Number of Shares	Weighted Average Exercise Price (per share)	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding at December 31, 2008	9,531	$ 8.16	4.2	$ 253
Granted	2,112	4.41		
Exercised	(110)	(3.93)		
Forfeited/cancelled/expired	(532)	(8.44)		
Outstanding at December 31, 2009	11,001	7.47	3.5	$6,503
Vested and exercisable at December 31, 2009	7,620	$ 8.80	3.1	$2,734
Expected to vest at December 31, 2009	10,727	$ 7.54	3.5	$6,208

Total intrinsic value of stock options exercised for the years ended December 31, 2009, 2008 and 2007 was $174, $534 and $1,211, respectively. Cash received from stock option exercises for the year ended December 31, 2009 was $433. Due to the Company's net loss position, no windfall tax benefits have been realized during the year ended December 31, 2009. As of December 31, 2009, approximately $6,808 of total unrecognized compensation cost related to unvested stock options is expected to be recognized over a weighted-average period of 2.1 years.

The following table summarizes information concerning options outstanding at December 31, 2009:

	Options Outstanding	Weighted Average Exercise Price (per share)	Weighted Average Remaining Contractual Term (in Years)	Options Exercisable
Exercise Price range (per share):				
$ 2.25 - $ 3.98	2,522	$ 3.71	3.9	958
$ 4.06 - $ 5.10	2,457	4.79	4.3	1,090
$ 5.22 - $ 6.49	2,411	5.88	3.1	1,966
$ 6.85 - $ 13.60	2,202	10.29	2.4	2,197
$ 13.65 - $ 20.30	1,409	17.18	3.6	1,409
	11,001	$ 7.47	3.5	7,620

Restricted Stock Units

In July 2006, the Compensation Committee authorized the issuance of restricted stock units ("RSUs") to each of the Company's then executive officers. The value of RSUs granted was based on the closing market price of the Company's common stock on the date of grant and is amortized on a straight-line basis over the five year requisite service period. A total of 195 RSUs were granted and had a total fair value at the date of grant of $811. The RSUs vest 20% annually over five years from the date of grant or earlier upon the event of a change in control. Any RSUs that have not vested at the time of termination of service to the Company are forfeited. The RSUs do not have voting rights, and the shares underlying the RSUs are not considered issued and outstanding until conversion. Any vested units will convert into an equivalent number of shares of common stock upon termination of employment with the Company.

(in thousands, except per share amounts)

The following table summarizes the Company's restricted stock unit activity:

	Number of Shares
Nonvested awards at December 31, 2008	105
Granted	—
Vested	(35)
Forfeited	—
Nonvested awards at December 31, 2009	70

Total fair value of RSUs vested during the years ended December 31, 2009, 2008 and 2007 were $146, $162 and $162, respectively. Approximately $209 of unrecognized share-based compensation expense related to unvested RSUs is expected to be recognized over the next 1.6 years.

12. Income Taxes

The Company had no federal, state or foreign income tax expense for the years ended December 31, 2009, 2008 and 2007.

Significant components of the Company's deferred tax assets and liabilities consist of the following:

	December 31,	
	2009	2008
Current deferred tax assets:		
Compensation related items	$ 307	$ 289
Accrued expenses and other	508	427
Noncurrent deferred tax assets:		
Accrued expenses and other	861	820
Domestic net operating loss carryforwards	125,234	116,945
Research and development credits	38,660	29,000
Property, equipment and intangible assets	7,666	6,693
Stock-based compensation	4,255	3,509
Contributions	434	434
Investments	234	413
Total deferred tax assets	178,159	158,530
Valuation allowance	(178,159)	(158,530)
Deferred tax assets	$ —	$ —

At December 31, 2009 and 2008, the Company provided a full valuation allowance against its net deferred tax assets since realization of these benefits could not be reasonably assured. The valuation allowance has increased $19,629, $25,321 and $23,201 for the years ended December 31, 2009, 2008 and 2007, respectively. The increase in the valuation allowance of $19,629 during the year ended December 31, 2009 resulted primarily from the generation of additional net operating loss carryforwards and research and development credits, partially offset by a reduction in deferred tax assets related to 2009 and prior years of $2,535 that are unlikely to be realized.

(in thousands, except per share amounts)

As of December 31, 2009, the Company had federal and state net operating loss carryforwards of $312,257 and $355,497, respectively. The net operating loss carryforwards expire in various amounts starting in 2009 and 2010 for federal and state tax purposes, respectively. The net operating loss carryforwards that expire in 2010 are not significant. The utilization of the federal net operating loss carryforwards may be subject to limitation under the rules regarding a change in stock ownership as determined by the Internal Revenue Code. If the Company's utilization of its net operating loss carryforwards is limited and the Company has taxable income which exceeds the permissible yearly net operating loss carryforward, the Company would incur a federal income tax liability even though its net operating loss carryforwards exceed its taxable income. Additionally, as of December 31, 2009 and 2008, the Company had federal research and development and orphan drug credit carryforwards of $38,660 and $29,000, respectively. The research and development carryforwards and orphan drug carryforwards begin to expire in varying amounts starting in 2011 and 2013, respectively.

On January 1, 2007, the Company adopted the provisions of FASB authoritative guidance related to accounting for uncertainty in income taxes. The guidance prescribes a recognition threshold and a measurement attribute for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more-likely-than-not to be sustained upon examination by taxing authorities. The amount recognized is measured as the largest amount of benefit that is greater than 50 percent likely of being realized upon ultimate settlement. At the adoption date of January 1, 2007, the Company had $110,008 of deferred tax assets, all of which was subject to a full valuation allowance, effectively reducing the deferred tax benefits to $0, since realization of these benefits could not be reasonably assured. As a result of adopting the guidance, the Company reduced its deferred tax assets by approximately $4,000 and reduced its full valuation allowance against the deferred tax assets by the same amount. Consequently, there was no impact to the Company's accumulated deficit upon adoption of the guidance. In conjunction with the adoption of the guidance, the Company did not recognize any amount for the payment of interest or penalties at January 1, 2007. During 2009 and 2008, the Company did not record any expense to the income statement for interest and penalties. The Company does not expect its unrecognized tax benefits to change significantly over the next 12 months.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	2009	2008
Balance at January 1	$ 8,388	$6,651
Additions to current year tax positions	2,442	1,689
Additions to tax positions of prior years	93	48
Balance at December 31	$10,923	$8,388

All of the Company's unrecognized tax benefits of $10,923 as of December 31, 2009, would, if recognized, reduce the Company's effective tax rate; however, currently all of the Company's deferred tax assets are subject to a full valuation allowance. The Company has no current pending or open tax examinations or audits. The Company is subject to tax examinations by U.S. Federal and state and local authorities for tax years subsequent to 2004. However, the net operating loss carryforwards and various research and development credits dating back to 1993 are open to adjustment by the taxing authorities.

(in thousands, except per share amounts)

Taxes computed at the statutory federal income tax rate of 35% (34% prior to 2008) are reconciled to the provision for income taxes as follows:

	Year Ended December 31,		
	2009	2008	2007
U.S. Federal tax at statutory rate	$(13,992)	$(20,685)	$(21,672)
State taxes (net of Federal benefit)	(1,619)	(2,140)	(2,810)
Change in valuation reserve	19,629	25,321	23,201
Research and development credit	(9,660)	(6,395)	(1,928)
NOL expiration	(308)	(22)	—
Reversal of the benefit booked in prior years	415	29	—
Nondeductible expenses due to credits	56	(3)	301
Other nondeductible expenses	5,479	3,895	2,908
Provision for income taxes	$ —	$ —	$ —

13. Collaboration Agreements

Allergan, Inc.

In December 2003, the Company entered into an agreement with Allergan to co-promote *Elestat* in the United States. Under the agreement, Inspire has the responsibility for promoting and marketing *Elestat* to ophthalmologists, optometrists and allergists in the United States and paying the associated costs. Inspire receives co-promotion revenue from Allergan on its U.S. net sales of *Elestat*. Allergan records sales of *Elestat* and is responsible for supply chain management, managed health care, customer order processing and regulatory compliance, as well as any international marketing and selling activities.

The *Elestat* co-promotion agreement provides that unless earlier terminated, the term of such agreement will be in effect until the earlier of (i) the approval and launch of the first generic epinastine product after expiration of the FDA exclusivity period covering *Elestat* in the United States, or (ii) the approval and launch of the first over-the-counter epinastine product after expiration of the listing of *Elestat* in the FDA's Orange Book. Following the termination of such co-promotion agreement, Inspire will no longer have rights to co-promote *Elestat*. Inspire will be entitled to receive post-termination payments from Allergan, based on any remaining net sales of *Elestat* for a period of 36 months. During the three successive 12-month periods immediately following the termination of the agreement, Allergan will be obligated to pay to Inspire 20%, 15% and 10%, respectively, on any net sales of *Elestat* in the United States.

Notices have been received from four companies, advising that each company filed an ANDA for a generic version of *Elestat*. The date of submission of the first ANDA filing to the FDA Office of Generic Drugs was October 14, 2008, according to the FDA's website (www.fda.gov).

Either Allergan or Inspire may terminate the agreement in the event of a material breach of the agreement by the other or in the event of the other's insolvency. Allergan can terminate the agreement upon a change of control where Inspire becomes an affiliate of a direct competitor of Allergan as that term is defined in the agreement. Inspire can terminate the agreement in the event that *Elestat* is withdrawn from the market for more than 90 days.

In June 2001, the Company entered into a joint license, development and marketing agreement with Allergan to develop and commercialize the Company's product candidate, *Prolacria*. The agreement also

provided the Company with revenue on net sales of Allergan's *Restasis*. Under the terms of the agreement, Allergan obtained an exclusive license to develop and commercialize *Prolacria* worldwide, with the exception of Japan and nine other Asian countries covered by Inspire's agreement with Santen Pharmaceutical Co., Ltd. ("Santen"). In return, Inspire received an up-front payment of $5,000 in 2001 on execution of the agreement and has received additional payments of $6,000 associated with the achievement of certain milestones. Inspire is entitled to receive up to an additional $28,000 in milestone payments assuming the successful completion of all the remaining milestones.

The Company is responsible for conducting, in collaboration with Allergan, the Phase 3 clinical trials needed to file a U.S. New Drug Application for *Prolacria*. Allergan is responsible for all other development activities under the agreement, including all development and regulatory activities needed for potential approval outside the United States and in its territories, and for ex-U.S. regulatory submissions, filings, and approvals relating to products. Allergan is responsible for all commercial costs except for the cost of Inspire's sales force in the United States. Allergan is required to use commercially reasonable efforts to conduct these development activities, seek ex-U.S. regulatory approvals and market and sell *Prolacria*.

The Company is also entitled to receive revenue from Allergan on net sales of *Restasis* and *Prolacria*, if any, worldwide, excluding most larger Asian markets. The Company began receiving revenue from net sales of *Restasis* in April 2004. In December 2008, the Company amended its agreement with Allergan such that the Company ceased co-promoting *Restasis* as of December 31, 2008. Notwithstanding the fact that the Company is no longer co-promoting *Restasis*, Allergan remains obligated to pay the Company royalties in relation to sales of *Restasis* at the rates in effect prior to the December 2008 amendment.

Unless earlier terminated pursuant to other terms of the agreement, the agreement will expire as to each product (*Restasis* or *Prolacria*, as the case may be) in each applicable country on the later of (i) the 10th anniversary of the first commercial sale of such product in the applicable country, or (ii) the date on which the sale of such product ceases to be covered by any claim of any applicable Inspire or Allergan patent. The agreement will expire in its entirety upon the expiration of the agreement with respect to all products in all countries as described in the previous sentence.

Cystic Fibrosis Foundation Therapeutics, Inc.

In October 2002, the Company entered into a study funding agreement with the Cystic Fibrosis Foundation Therapeutics, Inc. ("CFFT"), whereby the majority of the expenses for one Phase 2 clinical trial for denufosol for the treatment of cystic fibrosis were funded by the CFFT, but the Company also recorded the corresponding expenses and liabilities as the CFFT incurred these costs. This clinical trial was completed in 2004. If the Company receives FDA approval for denufosol for the treatment of cystic fibrosis, the Company will be obligated to pay a development milestone, and possibly a sales milestone, to the CFFT. The aggregate potential milestones under this agreement are approximately $16,000. The Company has recorded $1,915 of contingent liabilities in "Other long-term liabilities" associated with this agreement as of December 31, 2009 and 2008. If it does not receive FDA approval, the Company will have no financial obligation to the CFFT, including the Phase 2 clinical trial costs the CFFT funded on the Company's behalf.

InSite Vision Incorporated.

In February 2007, the Company entered into a license agreement with InSite Vision pursuant to which Inspire acquired exclusive rights to commercialize *AzaSite*, as well as other potential topical anti-infective products containing azithromycin as the sole active ingredient for use in the treatment of human ocular or

ophthalmic indications. The license agreement also grants Inspire exclusive rights to develop, make, use, market, commercialize and sell each product in the United States and Canada. Inspire is currently responsible for all regulatory obligations and strategies relating to the further development and commercialization of a product in the United States and Canada.

Pursuant to the license agreement, the Company paid an upfront licensing fee of $13,000. The Company paid an additional $19,000 milestone payment upon regulatory approval of *AzaSite* by the FDA. Additionally, the Company is obligated to pay a royalty on net sales of *AzaSite* for ocular infections in the United States and Canada. The royalty rate was 20% on net sales of *AzaSite* for the first two years of commercialization and in July 2009, the Company began paying a 25% royalty rate, which will continue for the duration of the agreement. The Company is obligated to pay royalties under the agreement for the longer of (i) 11 years from the launch of the subject product and (ii) the period during which a valid claim under a patent licensed from InSite Vision covers a subject product. Under the terms of the agreement, the Company's obligation to pay royalties to InSite Vision is subject to pre-determined minimum annual royalty payments. The determination of whether or not the Company will owe any such payments is based upon the amount of royalties accrued over a 12-month royalty period. There are five successive 12-month minimum royalty periods, the second of which commenced on October 1, 2009. The Company launched *AzaSite* in August 2007, and began paying royalties to InSite Vision in the fourth quarter of 2007.

Santen Pharmaceuticals Co., Ltd.

In December 1998, the Company entered into a development, license and supply agreement with Santen for the development of diquafosol tetrasodium for the therapeutic treatment of ocular surface diseases. Under the agreement, the Company granted Santen an exclusive license to develop and market diquafosol tetrasodium for ocular surface diseases in Japan, China, South Korea, the Philippines, Thailand, Vietnam, Taiwan, Singapore, Malaysia and Indonesia in the field. The Company is obligated to supply Santen with its requirements of diquafosol tetrasodium in bulk drug substance form for all preclinical studies, clinical trials and commercial requirements at agreed-upon prices.

Under the terms of the agreement, Inspire has received a total of $1,500 in equity and $3,000 in milestone payments, including a $1,250 milestone payment received in May 2008 and a $1,250 milestone payment received in March 2006. Depending on whether all milestones under the agreement are achieved, the Company could receive additional milestone payments of up to $1,750. In addition, the Company is entitled to receive royalties on net sales of diquafosol tetrasodium by Santen, if any.

The agreement will terminate when all patents licensed under the agreement have expired. Either Santen or the Company may terminate the agreement if the other materially breaches the agreement. In addition, the Company has the right to terminate the agreement at any time, subject to the coordinating committee's review and arbitration, if the Company determines that Santen has not made reasonably sufficient progress in the development or commercialization of potential products. If Santen breaches the agreement, or if the Company terminates the agreement because Santen has not made sufficient progress, Santen's license will terminate. Santen will provide the Company with all data and information relating to the Company's products, and will assign or permit it to cross-reference all regulatory filings and approvals.

Wisconsin Alumni Research Foundation

In November 2004, the Company licensed several patents for use in developing and commercializing new treatments for glaucoma from the Wisconsin Alumni Research Foundation ("WARF"). Under the terms of the

(in thousands, except per share amounts)

agreement, Inspire paid an upfront licensing payment of $150 in 2004 upon execution of the agreement and a $50 milestone payment related to the filing of an Investigational New Drug Application for its glaucoma program in 2006. The Company is obligated for additional contingent payments of up to an aggregate of $1,750 upon the achievement of development milestones, and royalties on sales of any regulatory approved product utilizing the licensed patents.

Inspire will design and fund all future research, development, testing, regulatory filings and potential marketing activities related to any product candidate under development or product developed from the license. Unless terminated earlier, the agreement will expire on a country-by-country basis upon the expiration of the patents in such country. The U.S. government may have limited rights in some of this patented technology. WARF may terminate the license if Inspire fails to make timely payment of any amount due to WARF under the agreement or commit a material breach of any material covenant contained in the agreement, subject to the right to cure.

14. Commitments and Contingencies

Operating Leases

Total rent expense for operating leases during 2009, 2008 and 2007 was $1,869, $2,098 and $1,813, respectively. Future minimum lease payments under non-cancelable operating leases as of December 31, 2009 are as follows:

Year Ending December 31,	Operating Leases
2010	$ 985
2011	203
2012	73
Total minimum lease payments	$1,261

The Company has entered into non-cancelable operating leases for its fleet of vehicles, facilities and office equipment that extend through 2012 and are subject to voluntary renewal options. The Company leases vehicles for its commercial organization under a Master Lease Agreement that allows for individual vehicle leases to be cancelable after one year. The Master Lease Agreement requires the Company to maintain a Standby Letter of Credit in the amount of $515 during the term of the lease. The vehicle Master Lease Agreement also requires that the vehicles under lease serve as collateral for the obligation.

Other Commitments

The Company has entered into contractual commitments or purchase obligations with various clinical research organizations, promotion and advertising agencies, manufacturers of active pharmaceutical ingredients and drug product for clinical and commercial use as well as with others. These financial commitments, which include both cancelable and non-cancelable arrangements, totaled approximately $17,489 as of December 31, 2009. Since many of these commitment amounts are dependent upon variable components of the agreements, actual payments and the timing of those payments may differ from management's estimates. In addition, the Company is obligated to pay royalties to InSite Vision as part of its license agreement for *AzaSite*. Under the terms of the agreement, the Company's obligation to pay royalties to InSite Vision is subject to pre-determined minimum annual royalty payments. The determination of whether or not the Company will owe any such payments is based upon the amount of royalties accrued over a 12-month royalty period. There are five

successive 12-month minimum royalty periods, the first of which commenced on October 1, 2008. The minimum royalties escalate each year. Remaining minimum royalties as of December 31, 2009 total $60,000.

Contingencies

As of December 31, 2009, the Company's existing license, collaboration and sponsored research agreements may require cash payments contingent upon the occurrence of certain future events. In the aggregate, these agreements may require payments of up to $21,350 assuming the achievement of all development milestones and up to an additional $4,000 assuming the achievement of all sales milestones. Amounts payable by the Company under these agreements are uncertain and are contingent on a number of factors, including the progress of its research, preclinical and development programs, its ability to obtain regulatory approvals, the commercial success of its approved products and future annual product sales levels. The Company is also obligated to pay royalties on net sales, if any, of certain product candidates currently in its portfolio. Some of the Company's license agreements require minimum annual license preservation fees.

15. Related Party Transactions

In February 2009, the Company entered into an agreement with Clinipace, Inc. ("Clinipace") for the provision of various data management and biostatistics services to support two Phase 2 clinical trials of *AzaSite* for the treatment of blepharitis. Under this agreement, the Company paid Clinipace $365 upon execution and is obligated to pay an additional $171 per month for 12 months commencing in March 2009. In addition, Clinipace has performed similar services in support of other development programs of the Company in 2009 and 2008, considered insignificant. The Company had expenses associated with Clinipace activities in 2009 and 2008, of $2,137 and $24, respectively. Kenneth B. Lee, Jr., the Chairman of the Company's Board of Directors, is a general partner of Hatteras Venture Partners, LLC, which owns approximately 28% of Clinipace. Christy Shaffer, the Company's President and Chief Executive Officer during 2009, also serves as a director of Clinipace. Neither Mr. Lee nor Dr. Shaffer have a personal interest in any amounts paid by the Company to Clinipace.

In August 2009, the Company completed a public offering of its common stock. Warburg participated in the public offering and acquired an additional 8,889 shares of common stock for total holdings of 22,907 shares of the Company's common stock, which represented approximately 28% of the Company's outstanding stock as of December 31, 2009. As part of the offering, the Company reimbursed Warburg for $500 of expenses incurred, related to their participation in the common stock sale. Prior to the sale of common stock in this offering, Warburg owned approximately 14,019, or 25%, of the then outstanding common stock of the Company. Jonathan S. Leff, serves as a member of the Company's Board of Directors and as a member of its Corporate Governance Committee. Since January 2000, he has served as a General Partner of Warburg, Pincus & Company, which is the managing partner of Warburg Pincus LLC, and as a Member and Managing Director of Warburg Pincus LLC, a private equity investment firm.

16. Employee Benefit Plan

The Company adopted a 401(k) Profit Sharing Plan ("the 401(k) Plan") covering all qualified employees on August 1, 1995. Participants may elect a salary reduction of 1% or more up to the IRS allowed maximum as a tax-deferred contribution to the 401(k) Plan. The 401(k) Plan permits discretionary employer contributions. If employer discretionary contributions are implemented, participants will begin vesting 100% immediately in such contributions. In 2009, 2008 and 2007, the Company elected a safe harbor contribution at 3.0% of annual compensation. These safe harbor contributions totaled $935, $938 and $752 for the years ended December 31, 2009, 2008 and 2007, respectively.

(in thousands, except per share amounts)

17. Revenue by Product Line

The Company operates its business as one operating segment. The Company derives all of its product revenue for *AzaSite* and all its co-promotion revenue for *Elestat* from product sales in the United States. Approximately 98% of royalty revenue for *Restasis* in fiscal years 2009, 2008 and 2007, was derived from product sales in the United States.

	Year ended December 31,		
	2009	2008	2007
Product Sales:			
AzaSite	$34,961	$18,349	$ 3,142
Co-Promotion and Royalty Sales:			
Restasis	38,445	32,761	24,442
Elestat	18,753	18,138	21,081
Total	$92,159	$69,248	$48,665

18. Quarterly Financial Data (unaudited)

	2009				
	First	Second	Third	Fourth	Total
Revenue	$ 14,331	$23,051	$25,168	$29,609	$ 92,159
Cost of sales	1,961	2,284	3,032	3,994	11,271
Net loss	(19,407)	(9,511)	(8,493)	(2,565)	(39,976)
Net loss per common share—basic and diluted	$ (0.34)	$ (0.17)	$ (0.12)	$ (0.03)	$ (0.60)

	2008				
Revenue	$ 9,703	$21,984	$19,952	$18,859	$ 70,498
Cost of sales	1,007	1,643	1,624	2,138	6,412
Net loss	(25,913)	(6,362)	(9,619)	(9,709)	(51,603)
Net loss per common share—basic and diluted	$ (0.46)	$ (0.11)	$ (0.17)	$ (0.17)	$ (0.91)

19. Subsequent Events

Appointment of Adrian Adams

Effective February 22, 2010, the Board of Directors (the "Board") of the Company appointed Adrian Adams as President and Chief Executive Officer of the Company, and as a member of the Board.

On February 18, 2010, the Company entered into an employment agreement (the "Employment Agreement") with Mr. Adams. The Employment Agreement provides for an initial term from February 22, 2010 to December 31, 2014.

Resignation of Christy L. Shaffer, Ph.D.

On February 19, 2010, the Company's Board of Directors received and accepted Christy L. Shaffer's resignation from the Company's Board of Directors and as President and Chief Executive Officer, effective February 22, 2010.

In connection with her resignation, Dr. Shaffer has entered into a Separation of Employment and Consulting Agreement, effective February 22, 2010 (the "Separation and Consulting Agreement") with the Company, pursuant to which she will provide consulting services to the Company for a period of twenty-four (24) months. The Separation and Consulting Agreement provides for: (i) a separation payment of $983; (ii) an award of 100 stock options; (iii) a stock award for 100 shares of the Company's common stock; and (iv) consulting payments, to be paid quarterly, at the annual rate of $468. The stock award and awards of stock options granted to Dr. Shaffer under the Separation and Consulting Agreement are fully vested and exercisable upon the grant date.

In addition, Dr. Shaffer's existing stock options with an exercise price equal to or less than $9.42 per share have been amended to provide that the exercise period for such options will be extended to the earlier of (i) the applicable award's expiration date, and (ii) February 22, 2013. All such options, to the extent unvested, became fully vested and exercisable. All of Dr. Shaffer's stock options with an exercise price greater than $9.42 per share were terminated on February 22, 2010. Additionally, all of Dr. Shaffer's existing unvested restricted stock units (20 units) became fully vested.

Exhibit Index

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation (Incorporated by reference to Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q filed on August 8, 2006).
3.2	Amended and Restated Bylaws (Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on December 18, 2007).
3.3	Certificate of Designations of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.3 to the Company's Annual Report on Form 10-K filed March 7, 2003).
3.4	Certificate of Amendment to Certificate of Designations of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 4.4 to the Company's Current Report on Form 8-K filed on July 23, 2007).
3.5	Certificate of Designations, Number, Voting Powers, Preferences and Rights of Series A Exchangeable Preferred Stock of Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 4.3 to the Company's Current Report on Form 8-K filed on July 23, 2007).
3.6	Certificate of Retirement of Series A Exchangeable Preferred Stock of Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on December 21, 2007).
4.1	Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
4.2	Rights Agreement, dated as of October 21, 2002, between the Company and Computershare Trust Company, which includes the form of Certificate of Designation of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. as Exhibit "A", the form of Rights Certificate as Exhibit "B" and the Summary of Rights to Purchase Preferred Stock as Exhibit "C" (Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on October 22, 2002).
4.3	First Amendment to Rights Agreement, dated July 17, 2007, by and between Inspire Pharmaceuticals, Inc. and Computershare Trust Company (Incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on July 23, 2007).
10.1†	Inspire Pharmaceuticals, Inc. Amended and Restated 1995 Stock Plan, as amended (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on April 21, 2005).
10.2†	Form of Incentive Stock Option (Incorporated by reference to Exhibit 10.2 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.3*	Development, License and Supply Agreement between Inspire Pharmaceuticals, Inc. and Santen Pharmaceutical Co., Ltd., dated as of December 16, 1998 (Incorporated by reference to Exhibit 10.15 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.4†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Benjamin R. Yerxa dated February 4, 2000 (Incorporated by reference to Exhibit 10.26 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.5†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Christy L. Shaffer dated February 10, 2000 (Incorporated by reference to Exhibit 10.28 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).

Exhibit Number	Description
10.6†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Joseph Schachle dated April 3, 2001 (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 10, 2001).
10.7*	License, Development and Marketing Agreement between Inspire Pharmaceuticals, Inc. and Allergan, Inc., dated as of June 22, 2001 (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 29, 2001).
10.8*	Study Funding Agreement, dated as of October 3, 2002, between Inspire Pharmaceuticals, Inc. and The Cystic Fibrosis Foundation Therapeutics, Inc. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 4, 2002).
10.9†	Form of Inspire Pharmaceuticals, Inc. Employee Stock Option Agreement (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.10†	Form of Inspire Pharmaceuticals, Inc. Director Non-Statutory Stock Option Agreement (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.11*	First Amendment to License, Development and Marketing Agreement, dated December 8, 2003, between Inspire Pharmaceuticals, Inc. and Allergan, Inc. and Allergan Sales, LLC and Allergan Pharmaceuticals Holdings (Ireland) Ltd. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 9, 2003).
10.12*	Elestat (Epinastine) Co-Promotion Agreement, entered into as of December 8, 2003, by and between Allergan Sales, LLC and Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 1, 2004).
10.13†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Thomas R. Staab, II, dated May 16, 2003 (Incorporated by reference to Exhibit 10.35 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.14	Master Lease Agreement between GE Capital Fleet Services and Inspire Pharmaceuticals, Inc., dated as of November 18, 2003, and related documentation (Incorporated by reference to Exhibit 10.38 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.15	Master Security Agreement between General Electric Capital Corporation and Inspire Pharmaceuticals, Inc., dated as of November 12, 2003, and related documentation (Incorporated by reference to Exhibit 10.39 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.16†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between the Company and R. Kim Brazzell, dated August 5, 2004 (Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed November 9, 2004).
10.17*	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and the Wisconsin Alumni Research Foundation, effective November 2, 2004 (Incorporated by reference to Exhibit 10.44 to the Company's Annual Report on Form 10-K filed March 11, 2005).
10.18†	Form of Inspire Pharmaceuticals, Inc. Employee Stock Option Agreement (Incorporated by reference to Exhibit 10.56 to the Company's Annual Report on Form 10-K filed March 11, 2005).
10.19†	Form of Incentive Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on June 16, 2005).
10.20†	Form of Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed on June 16, 2005).
10.21†	Form of Director's Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed on June 16, 2005).

Exhibit Number	Description
10.22†	Form of Stock Appreciation Right Grant Agreement (Incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed on June 16, 2005).
10.23†	Form of Stock Award Grant Agreement (Incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed on June 16, 2005).
10.24†	Form of Restricted Stock Unit Agreement (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 7, 2006).
10.25	Amended and Restated Lease Agreement, dated as of November 30, 2006, by and between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC with respect to certain premises located within the Royal Center I building at 4222 Emperor Blvd., Durham, North Carolina (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 6, 2006).
10.26	Amended and Restated Lease Agreement, dated as of November 30, 2006, by and between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC with respect to certain premises located within the Royal Center II building at 4222 Emperor Blvd., Durham, North Carolina (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on December 6, 2006).
10.27†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Joseph M. Spagnardi, dated May 10, 2005 (Incorporated by reference to Exhibit 10.43 to the Company's Annual Report on Form 10-K filed on March 16, 2007).
10.28	Loan and Security Agreement, dated as of December 22, 2006, among Inspire Pharmaceuticals, Inc., Merrill Lynch Capital and Silicon Valley Bank (Incorporated by reference to Exhibit 10.45 to the Company's Annual Report on Form 10-K filed on March 16, 2007).
10.29*	License Agreement by and between Inspire Pharmaceuticals, Inc. and InSite Vision Incorporated, dated as of February 15, 2007 (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.30*	Supply Agreement by and between Inspire Pharmaceuticals, Inc. and InSite Vision Incorporated, dated as of February 15, 2007 (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.31	Trademark License Agreement by and between Inspire Pharmaceuticals, Inc. and InSite Vision Incorporated, dated as of February 15, 2007 (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.32	Side Letter by and between Inspire Pharmaceuticals, Inc., InSite Vision Incorporated and Pfizer Inc., dated as of February 15, 2007 (Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.33†	Form of Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.34†	Form of Director's Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.35†	Executive Officer Annual Cash Bonus Plan (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 13, 2007).
10.36	Standstill Agreement, dated July 20, 2007, among Inspire Pharmaceuticals, Inc., Warburg Pincus Private Equity IX, L.P., Warburg Pincus IX, LLC, Warburg Pincus Partners, LLC and Warburg Pincus & Co. (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on July 23, 2007).
10.37	First Amendment to Loan and Security Agreement by and among Merrill Lynch Capital, Silicon Valley Bank, and Inspire Pharmaceuticals, Inc., dated as of June 27, 2007 (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2007).

Exhibit Number	Description
10.38†	Amended and Restated 2005 Equity Compensation Plan (Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2007).
10.39*	Manufacturing Services Agreement, dated September 11, 2007, by and between Inspire Pharmaceuticals, Inc. and Catalent Pharma Solutions, LLC (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on November 9, 2007).
10.40†	Executive Change in Control Severance Benefit Plan, effective as of March 29, 2008 (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 9, 2008).
10.41†	Change in Control Severance Benefit Plan, amended and restated as of March 29, 2008 (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on May 9, 2008).
10.42	Second Amendment to License, Development and Marketing Agreement, dated December 24, 2008, between Inspire Pharmaceuticals, Inc. and Allergan, Inc., Allergan Sales, LLC and Allergan Pharmaceuticals Holdings (Ireland) Ltd. (Incorporated by reference to Exhibit 10.62 to the Company's Annual Report on Form 10-K filed on March 13, 2009).
10.43†	Amended and Restated Director Compensation Policy dated March 1, 2009 (Incorporated by reference to Exhibit 10.63 to the Company's Annual Report on Form 10-K filed on March 13, 2009).
10.44†	Inspire Pharmaceuticals, Inc. Executive Change in Control Severance Benefit Plan, Amended and Restated as of July 8, 2009 (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.45†	Inspire Pharmaceuticals, Inc. Change in Control Severance Benefit Plan, Amended and Restated as of July 8, 2009 (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.46†	Inspire Pharmaceuticals, Inc. Amended and Restated 2005 Equity Compensation Plan, as amended effective July 8, 2009 (Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.47†	Form of 1995 Stock Plan Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.48†	Form of Restricted Stock Unit Agreement Under the Amended and Restated 2005 Equity Compensation Plan (Incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.49†	Form of Inspire Pharmaceuticals, Inc. 1995 Stock Plan Director's Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.50†	Form of Inspire Pharmaceuticals, Inc. 2005 Equity Compensation Plan Director's Nonqualified Stock Option Grant Agreement (Incorporated by reference to Exhibit 10.7 to the Company's Current Report on Form 8-K filed on July 13, 2009).
10.51	Amendment No. 1 to Standstill Agreement, dated August 4, 2009, between Inspire Pharmaceuticals, Inc. and Warburg Pincus Private Equity IX, L.P. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on August 10, 2009).
10.52	Technology License Agreement For the Manufacture of Denufosol, dated as of October 2, 2009, between Inspire Pharmaceuticals, Inc. and Yamasa Corporation, with an effective date of September 25, 2009 (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 10-Q filed on November 6, 2009).
10.53†	Executive Incentive Compensation Recovery ("Clawback") Policy, dated December 18, 2009.

Exhibit Number	Description
10.54†	Amended and Restated Equity Compensation Grant Policy, dated December 18, 2009.
10.55†	Amended and Restated Director Compensation Policy, dated December 18, 2009.
10.56†	Executive Employment Agreement, between Inspire Pharmaceuticals, Inc. and Adrian Adams, made as of February 18, 2010 (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on February 24, 2010).
10.57†	Stock Option Agreement by and between Inspire Pharmaceuticals, Inc. and Adrian Adams, effective as of February 22, 2010 (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on February 24, 2010).
10.58†	Separation of Employment and Consulting Agreement between Inspire Pharmaceuticals, Inc. and Dr. Christy L. Shaffer, Ph.D., made as of February 19, 2010 (Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed on February 24, 2010).
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

---

* Confidential treatment has been granted with respect to a portion of this Exhibit.

** Confidential treatment has been requested with respect to a portion of this Exhibit.

† Denotes a management contract or compensation plan or arrangement required to be filed as an exhibit pursuant to Item 15(c) of this Form 10-K.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-147733 and 333-141169) and Form S-8 (Nos. 333-56360, 333-130496 and 333-148185) of Inspire Pharmaceuticals, Inc. of our report dated March 15, 2010 relating to the financial statements, financial statement schedule and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
March 15, 2010

Exhibit 31.1

INSPIRE PHARMACEUTICALS, INC.

CERTIFICATIONS

I, Adrian Adams, certify that:

1. I have reviewed this annual report on Form 10-K of Inspire Pharmaceuticals, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 15, 2010

/s/ ADRIAN ADAMS

Adrian Adams
President & Chief Executive Officer
(principal executive officer)

Exhibit 31.2

INSPIRE PHARMACEUTICALS, INC.

CERTIFICATIONS

I, Thomas R. Staab, II, certify that:

1. I have reviewed this annual report on Form 10-K of Inspire Pharmaceuticals, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 15, 2010

/s/ THOMAS R. STAAB, II

Thomas R. Staab, II
Chief Financial Officer
(principal financial officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the annual report of Inspire Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2009, as filed with the Securities and Exchange Commission (the "Report"), I, Adrian Adams, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 15, 2010

/s/ ADRIAN ADAMS

Adrian Adams
President & Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the annual report of Inspire Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2009, as filed with the Securities and Exchange Commission (the "Report"), I, Thomas R. Staab, II, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 15, 2010

/s/ THOMAS R. STAAB, II

Thomas R. Staab, II
Chief Financial Officer
(principal financial officer)

CORPORATE INFORMATION

CORPORATE OFFICERS

Adrian Adams
President and Chief Executive Officer

R. Kim Brazzell, Ph.D.
Executive Vice President
Head, Ophthalmology Business

Joseph K. Schachle
Executive Vice President
Chief, Commercial and Corporate Operations

Joseph M. Spagnardi
Senior Vice President
General Counsel and Secretary

Thomas R. Staab, II
Executive Vice President
Chief Financial Officer and Treasurer

Benjamin R. Yerxa, Ph.D.
Executive Vice President
Chief, Research and Development

BOARD OF DIRECTORS

George B. Abercrombie (1)
Former President and Chief Executive Officer
Hoffmann-La Roche Inc.

Adrian Adams
President and Chief Executive Officer
Inspire Pharmaceuticals, Inc.

Kip A. Frey (1) (3)
President and CEO
Zenph Sound Innovations, Inc.
Adjunct Professor, Duke University

Alan F. Holmer (1) (3)
Former Special Envoy to China
Former President and Chief Executive Officer
Pharmaceutical Research and Manufacturers of America (PhRMA)

Nancy J. Hutson, Ph.D. (2) (4)
Former Senior Vice President
Global Research and Development
Pfizer Inc.

Richard S. Kent, M.D. (2) (4)
Venture Partner
Intersouth Partners

Kenneth B. Lee, Jr. (1) (2)
Chairman
Inspire Pharmaceuticals, Inc.
General Partner
Hatteras Venture Partners, L.L.C.

Jonathan S. Leff (3)
Managing Director
Warburg Pincus, L.L.C

CORPORATE HEADQUARTERS

Inspire Pharmaceuticals, Inc.
4222 Emperor Boulevard, Suite 200
Durham, NC 27703
www.inspirepharm.com
Ph: 919-941-9777 Fax: 919-941-9797

SECURITIES INFORMATION

Exchange: NASDAQ Global Market℠
Symbol: ISPH

ANNUAL MEETING

Inspire's Annual Meeting of Stockholders will be held on Thursday, June 3, 2010, at 8:00 a.m. E.T. at Inspire Pharmaceuticals, Inc., 4222 Emperor Blvd., Suite 200, Durham, NC 27703.

STOCKHOLDER INFORMATION

Copies of the Company's Form 10-K, Form 10-Q, quarterly earnings release, or other information may be obtained free of charge through the corporate website, www.inspirepharm.com, or by calling 919-941-9777.

TRANSFER AGENT

Computershare Trust Company, N.A.
250 Royall Street
Canton, MA 02021
www.computershare.com
Toll free: 800-962-4284
Fax: 312-601-2312

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

PricewaterhouseCoopers LLP
150 Fayetteville Street, Suite 2300
Raleigh, NC 27601

CORPORATE COUNSEL

Reed Smith LLP
Princeton Forrestal Village
136 Main Street, Suite 250
Princeton, NJ 08540

(1) Audit Committee member
(2) Compensation Committee member
(3) Corporate Governance Committee member
(4) Development Committee member

FORWARD-LOOKING STATEMENTS

This document contains forward-looking statements that present our expectations and plans regarding future performance, and these statements are subject to significant risks and uncertainties that could affect our future performance, including those relating to product development. Actual results could differ materially from those described herein. Information on various factors that could affect our results is detailed in our reports filed with the Securities and Exchange Commission.

4222 Emperor Boulevard
Suite 200
Durham, NC 27703
(919) 941-9777
www.inspirepharm.com