INSPIRE

2008 ANNUAL REPORT

To Our Stockholders,

During 2008, we delivered double-digit revenue growth, achieved important clinical milestones and applied prudent financial management to our operations. Based on this progress, Inspire is well positioned to build stockholder value by moving forward with the clinical development of multiple late-stage novel programs and generating an attractive revenue stream from marketed products.

Generating Double-Digit Revenue Growth

We reached $70.5 million in total 2008 revenues, a 45% increase from the prior year, driven primarily by *AzaSite*® and *Restasis*® sales. We generated $18.3 million in revenues from the promotion of *AzaSite* as well as $18.1 million and $32.8 of co-promotion revenue based on net sales of *Elestat*® and *Restasis*, respectively. We maintained tight control over operating expenses, limiting total growth to less than 5% over 2007. Our operating expenses for the year ended December 31, 2008 were $120.2 million and we had a net loss of $51.6 million or ($0.91) per common share for the year. We ended 2008 with cash and investments of $73.0 million that should fund our operations into 2010, which is especially important given the current economic conditions.

Driving Innovative Pipeline Progress

Over the past year, we completed multiple clinical trials that enabled us to make critical pipeline decisions. We also began publishing and presenting this data in key scientific forums. Here is a snapshot of the major clinical developments in 2008 and early 2009:

- Cystic Fibrosis – We announced that TIGER-1, our first pivotal Phase 3 trial of denufosol tetrasodium for cystic fibrosis, demonstrated statistical significance for its primary efficacy endpoint. We presented data from this trial at the preeminent North American cystic fibrosis medical conference. The TIGER-1 trial included a 24-week placebo-controlled period followed by a 24-week open-label safety extension. Patients who continued to receive denufosol for an additional 24 weeks during the open-label extension experienced a progressive improvement in lung function. We initiated TIGER-2, our second pivotal Phase 3 trial, which is designed with a longer placebo-controlled period of 48 weeks, and have been enrolling patients at clinical sites in the United States, Canada, Australia and New Zealand.
- Dry Eye – We worked with the dry eye medical community, our partner, Allergan, Inc., and the U.S. Food and Drug Administration (FDA) to determine next steps for *Prolacria*™ (diquafosol tetrasodium) for dry eye. We were able to reach agreement on a trial design with the FDA through the Special Protocol Assessment process and, in early 2009, initiated a pivotal Phase 3 environmental trial with the primary efficacy endpoint of reduction of central corneal staining scores to zero from a baseline score of three, using the National Eye Institute scale. In 2008, our Asian partner, Santen Pharmaceutical Co., Ltd., filed an application with Japanese regulators for marketing approval of its formulation of diquafosol, which it refers to as DE-089.
- Blepharitis – Last year, we conducted a series of small, open-label Phase 4 clinical trials in which use of *AzaSite* showed treatment benefit in patients with blepharitis, a common ocular surface disease with limited current treatment options. In order to best leverage this opportunity, we evaluated our Phase 4 data, conducted market research, assessed the potential commercial opportunity and sought input from medical experts. Based on this analysis, we decided to pursue an additional indication for blepharitis by initiating a Phase 2 program in 2009.
- Glaucoma – We are completing Phase 1 proof-of-concept clinical trials testing in two compounds in glaucoma patients to evaluate safety, tolerability and intraocular pressure lowering effects.

Other Developments

We completed an initial Phase 3 trial of epinastine nasal spray for allergic rhinitis that did not meet its primary endpoint. Our analysis of the overall data in this program and the current competitive environment in allergic rhinitis indicated that epinastine nasal spray did not show potential to meet our desired product profile and thus we discontinued further development.

Creating Value in 2009 and Beyond

As we begin 2009, we see many opportunities for future value creation, including four potential product approvals and launches in the next several years: *Prolacria* for dry eye in the United States; Santen's DE-089 diquafosol candidate for dry eye in Japan; denufosol for cystic fibrosis in the United States; and *AzaSite* for blepharitis in the United States. These opportunities represent our highest development priorities and are the current focus of our 2009 plans and our three year longer-term outlook.

Specifically, in 2009, our team plans to focus on the following activities: continuing double-digit revenue growth, completing enrollment in the TIGER-2 cystic fibrosis trial, enrolling the pivotal *Prolacria* trial, and pursuing a new *AzaSite* indication for the treatment of blepharitis by initiating a Phase 2 clinical program.

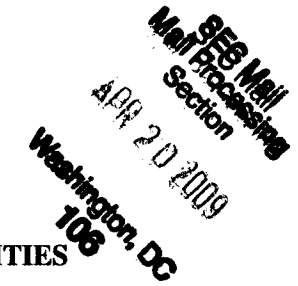
We closely monitor the business environment in which we operate, with particular attention to economic, regulatory and political developments. Given the current challenging economic and capital-raising environment, we are focusing resources on our late-stage clinical programs and revenue-generating marketed products. As a result, in the near-term, we will not be funding early pre-clinical discovery research. We appreciate the important contribution of our scientists and others who helped lay the foundation of the clinical development pipeline we have today.

We remain optimistic about our opportunities for value creation based on advancing our late-stage clinical development pipeline and utilizing our commercial capabilities to generate revenue growth. We believe our strategy of developing and commercializing novel and needed prescription pharmaceutical products for ophthalmic and pulmonary diseases will differentiate us from our peers and provide long-term value for our stockholders.

Sincerely,

Christy L. Shaffer, Ph.D.
President and CEO
Inspire Pharmaceuticals, Inc.

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, 2008

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. ~~000-51135~~ 1-31577

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 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. $180,686,731

Indicate the number of shares outstanding of each of the Registrant's classes of common stock, as of January 31, 2009.

Class	**Number of Shares**
Common Stock, $.001 par value	56,680,167

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, 2008 are incorporated by reference into Part III of this report.	Items 10, 11, 12, 13, 14

INSPIRE PHARMACEUTICALS, INC.
2008 FORM 10-K ANNUAL REPORT

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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 *Prolacria* for dry eye and denufosol tetrasodium for cystic fibrosis, which are both in Phase 3 development and *AzaSite* for blepharitis, which is beginning Phase 2 development. We receive revenues 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 royalties (2)
Product Candidates in Clinical Development			
Prolacria (diquafosol tetrasodium)	Dry eye disease	Allergan; Santen Pharmaceutical	Phase 3 (3)
Denufosol tetrasodium	Cystic fibrosis	None	Phase 3
AzaSite	Blepharitis	InSite Vision	Initiating Phase 2 program
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) Under our agreement with Allergan, the royalty 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, Taiwan, Korea, Hong Kong and China.

(3) In June 2003, we filed an NDA with the FDA for *Prolacria* for the treatment of dry eye disease. We have received two approvable letters from the FDA (in December 2003 and December 2005). Additionally, Santen filed an application for manufacturing and marketing approval of a different formulation of diquafosol tetrasodium with the Japanese Ministry of Health, Labor and Welfare on May 30, 2008.

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*, 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 grants us exclusive rights to develop, make, use, market, commercialize and sell the products 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 that expire in March 2019.

Market Opportunity. The U.S. single-entity ocular antibiotic market was approximately $411 million for the 12 months ended December 31, 2008 according to data compiled from IMS Health. Total prescriptions for all products in the ocular antibiotic market were approximately 14.8 million for the 12 months ended December 31, 2008, a decrease of approximately 1% from the prior year according to data compiled from IMS Health.

Elestat

Elestat (epinastine HCl ophthalmic solution) 0.05%, a topical antihistamine with mast cell stabilizing and anti-inflammatory activity, was 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, is indicated for adults and children at least three years old, and is administered through one drop in each eye twice-a-day. *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.

In December 2003, we entered into an agreement with Allergan to co-promote *Elestat* in the United States and launched *Elestat* in the United States in February 2004. 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 other product costs. 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 attributable to *Elestat* will be minimal. See "—Collaborative Agreements—*Allergan, Inc.—Elestat.*"

On September 30, 2008, the U.S. Patent and Trademark Office, or USPTO, issued a method of treatment patent related to *Elestat* (the "*Elestat* Patent") to an affiliate of Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, the developer of the invention. Notwithstanding the fact that the *Elestat* Patent was issued by the USPTO, subject to applicable law, competitors are permitted to submit to the FDA an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) application 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 ANDA filing to the FDA Office of Generic Drugs was October 14, 2008, according to the FDA's website (www.fda.gov). We have been further notified by Allergan that Boehringer Ingelheim has decided not to file infringement lawsuits against the ANDA filers. Boehringer Ingelheim is the owner of the *Elestat* Patent and we do not have a license to the *Elestat* Patent.

We plan to continue co-promoting and receiving co-promotion revenues on *Elestat* sales during the FDA's review period of these ANDAs, which we currently expect to continue beyond 2009. 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 attributable to Elestat will be minimal*"—for further discussion of the risk related to the ANDA filings pertaining to a generic version of *Elestat*.

Market Opportunity. The 2008 annual U.S. market for current prescription ocular allergy products was approximately $505 million, and has experienced a decline, in terms of dollars, of approximately 2% over 2007, based on data compiled and reported by IMS Health, as of December 31, 2008. In terms of prescriptions, the total U.S. allergic conjunctivitis market decreased approximately 7% for the year ended December 31, 2008, according to data compiled from IMS Health. For the years ended December 31, 2008, 2007 and 2006, we recognized approximately $18.1 million, $21.1 million and $20.3 million, respectively, of revenue from net sales of *Elestat*.

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 provided us with a royalty on worldwide (except most Asian markets) net sales of Allergan's *Restasis* and granted us the right to co-promote *Restasis* in the United States. In January 2004, we began co-promotion of *Restasis* to eye care professionals and allergists in the United States. We began receiving co-promotion revenue on Allergan's net sales of *Restasis* in April 2004.

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 sales of *Restasis* at the rates in effect prior to the December 2008 amendment. See "—Collaborative Agreements—*Allergan, Inc.—Restasis and Prolacria.*"

The manufacture and sale of *Restasis* is protected in the United States under a use patent that expires in August 2009 and a formulation patent that expires in May 2014.

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. Since dry eye disease is more prevalent among the elderly and post-menopausal women, this market is expected to grow as populations age. We estimate, based on an extrapolation from U.S. data, that dry eye disease affects over 30 million people in the eight major international prescription pharmaceutical markets, of which over nine million are in North America. For the years ended December 31, 2008, 2007 and 2006, Allergan has recognized approximately $444 million, $345 million and $270 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

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

Overview. Diquafosol tetrasodium is a dinucleotide that we discovered, 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.

We are developing *Prolacria* as an eye drop for dry eye disease. Since *Prolacria* and *Restasis* have different mechanisms of action, we consider them complementary products and, if *Prolacria* is approved by the FDA, we believe there is commercial opportunity for both of these products. 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 and when we receive FDA approval and *Prolacria* is launched, we expect to begin co-promoting this product. Pursuant to this agreement, Allergan is responsible for obtaining regulatory approval of diquafosol tetrasodium in Europe. See "—Collaborative Agreements—*Allergan, Inc.—Restasis and Prolacria.*"

Development Status. In June 2003, we filed a New Drug Application, or NDA, with the FDA for *Prolacria* for the treatment of dry eye disease. We have received two approvable letters from the FDA (in December 2003 and December 2005). Subsequently, we have held meetings with the FDA and conducted various studies to facilitate a clinical trial design that both the FDA and Inspire agree is appropriate and reasonable to continue our clinical development of *Prolacria.*

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.* In January 2009, we reached agreement with the FDA on the design of a Phase 3 clinical trial for *Prolacria* and initiated enrollment in the trial.

Based on the SPA agreement, we have initiated a Phase 3, randomized, placebo-controlled, environmental clinical trial (Trial 03-113) to evaluate the efficacy and safety of *Prolacria* in approximately 450 subjects with dry eye disease who have a fluorescein staining score of three in the central region of the cornea at baseline, using the National Eye Institute (NEI) scale of zero to three. Subjects will be randomized to *Prolacria* or placebo administered as eye drops four-times daily for six weeks at approximately 60 U.S. and Canadian sites. At the end of February 2009, there were approximately 47 patients enrolled and randomized in the trial and more than two-thirds of the targeted 60 clinical sites able to enroll patients.

The agreed upon primary efficacy endpoint in Trial 03-113 is the proportion of subjects receiving *Prolacria* that achieve clearing of fluorescein staining of the central region of the cornea in the study eye (a score of zero on the NEI scale) at the six-week trial endpoint, compared to those receiving placebo. The FDA indicated, as part of the SPA review process, that even if this clinical trial is successful, the FDA's review of the NDA for *Prolacria* will also take into account the robustness of the trial results, that a surrogate endpoint was used, the results from previous *Prolacria* trials and the overall risk/benefit.

Estimated subsequent costs necessary to amend our NDA submission for *Prolacria* and resubmit the application for commercial approval in the United States are projected to be in the range of $10 million to $15 million. This range includes costs for completing Trial 03-113, regulatory and consulting activities, salaries for development personnel, and other unallocated development costs, but excludes the cost of pre-launch inventory which is Allergan's responsibility. If we are required to do more than one additional Phase 3 clinical trial, our costs will likely be higher than the projected range. The projected costs associated with *Prolacria* are difficult to determine due to the uncertainty of the FDA's scientific review and interpretation of what is required to demonstrate safety and efficacy sufficient for approval. Actual costs could be materially different from our estimate. For a more detailed discussion of the risks associated with the development of *Prolacria* and our other development programs, including factors that could result in a delay of a program and increased costs associated with such a delay, please see the Risk Factors described elsewhere in this report.

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 completed its Phase 3 clinical testing of DE-089, for which we received a related milestone payment of $1.25 million. 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. See "—Collaborative Agreements-*Santen Pharmaceutical Co., Ltd.*"

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. We believe that our product candidate could be the first FDA approved product that mitigates the underlying ion transport 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. Denufosol is designed to enhance the lung's innate mucosal hydration and mucociliary clearance mechanisms, which in cystic fibrosis patients are impaired due to a genetic defect. By hydrating airways and stimulating mucociliary clearance through activation of the $P2Y_2$ receptor, denufosol can potentially help keep the lungs of cystic fibrosis patients clear of thickened mucus, reduce infections and limit the damage that occurs as a consequence of the prolonged retention of thick and tacky infected secretions. 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) 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) $\geq$ 75%) at clinical centers across North America. This portion of the clinical trial was followed by a 24-week open-label denufosol safety extension in approximately 300 patients.

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, $p = 0.072$). There were no statistically significant differences between denufosol and placebo relative to the frequency of pulmonary exacerbations.

In late 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 open-label extension 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 open-label safety extension, 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 open-label extension. 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. There was an approximate 95% completion rate of the patients who entered the open-label extension. We expect to receive and analyze results from the open-label extension of TIGER-1 by the second quarter of 2009.

TIGER-2: In February 2008, we initiated patient enrollment in TIGER-2, our second planned pivotal Phase 3 clinical trial, and in July 2008, we announced modifications to the clinical protocol for this ongoing clinical trial. The key changes to the protocol were: (i) increasing the length of the placebo-controlled portion of the trial from 24 to 48 weeks, such that the primary efficacy endpoint is the change from baseline in FEV_1 at the 48-week trial endpoint; (ii) increasing the target enrollment from 350 patients to approximately 450 patients; and (iii) modifying entrance criteria to add an upper limit to the lung function criteria (targeting patients with a baseline $FEV_1 \geq 75\%$ and $\leq 110\%$ predicted normal). In consultation with key experts, we determined that a longer treatment period of 48 weeks is appropriate based on the progressive improvement from baseline in FEV_1 observed in patients who received denufosol in both the 24-week, placebo-controlled period of TIGER-1, as well as the 24-week open-label safety extension. 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 currently expect to have approximately 100 participating clinical trial sites across the United States, Canada, Australia and New Zealand. At the end of February 2009, we had 229 patients enrolled. We are targeting completion of TIGER-2 enrollment in 2009. The availability of TIGER-2 results will be dependent on the rate of enrollment in the clinical trial, but will likely follow receipt of the final study report of the ongoing two-year carcinogenicity study in rodents (discussed below). There are several patients who have recently completed TIGER-2 and all of those patients have elected to participate in the follow-on study. This follow-on study is an open-label denufosol-only 48-week clinical trial that we are offering to all the patients who successfully complete TIGER-2.

Other. In 2006, we completed a 52-week inhalation toxicology study in one animal species, and we 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 addition, in November 2006, we initiated the required two-year inhalation

carcinogenicity study in rats. The in-life dosing phase of the study has been completed and the data analysis is ongoing. This carcinogenicity study must be completed prior to submitting an NDA filing. The time from initiation of this study to receipt of the final study report is expected to be up to three years. We expect to receive the final study report for this carcinogenicity study in the second half of 2009.

Estimated subsequent costs necessary to submit an NDA for denufosol for the treatment of cystic fibrosis are projected to be in the range of $35 million to $45 million. This estimate includes completing TIGER-2, the subsequent open-label trial and the carcinogenicity study, 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, but excludes costs to secure a secondary supplier for denufosol, the cost of pre-launch inventory and any product approval milestones payable to the Cystic Fibrosis Foundation Therapeutics, Inc., or the 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, toxicology and carcinogenicity 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, other parties may assist in the funding of our development costs, and an anticipated NDA filing could be delayed. For a more detailed discussion of the risks associated with our development programs, please see the Risk Factors described elsewhere in this report.

We intend to participate in the commercialization in North America for denufosol for the treatment of cystic fibrosis. We are seeking to secure a corporate partner to develop and commercialize this product candidate outside of North America. We are also in discussions with additional third-party manufacturers for the purpose of establishing a secondary source of supply for denufosol.

Market Opportunity. The current 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. Annual sales in the United States of the two prescription pharmaceutical products to treat cystic fibrosis lung disease, *Pulmozyme* and *TOBI*, were approximately $302 million and $238 million, respectively, based on data compiled and reported by IMS Health as of December 31, 2008.

AzaSite for the treatment of blepharitis

Overview. We have decided to initiate a clinical program to pursue a potential new indication for *AzaSite* for the treatment of blepharitis. Blepharitis is a common ocular condition characterized by inflammation of the eyelids and associated signs and symptoms, which are often secondary to infection. 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. We received positive results from several small open-label Phase 4 clinical trials. Based upon our own market research as well as input from eye care specialists, blepharitis is a very common disease. There are limited treatment options and no prescription pharmaceutical products indicated for the treatment of this disease.

Development Status. 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 and the potential commercial opportunity. In addition, we have had preliminary discussions with the FDA on potential regulatory pathways.

Based on preliminary information gathered to date, we have decided to pursue a Phase 2 program to study *AzaSite* for the treatment of blepharitis. We plan to initiate two Phase 2 placebo-controlled clinical trials in the second quarter of 2009 and we expect to have data available in early 2010.

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 that may be 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 several patents for use in developing and commercializing new treatments for glaucoma from Wisconsin Alumni Research Foundation, or WARF. See "—Collaborative Agreements—*Wisconsin Alumni Research Foundation.*" Under the technology licensed from WARF, 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 (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 dose-ranging clinical trial 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 clinical trial for a second compound referred to as INS117548. The placebo-controlled, dose-escalating trial is designed to evaluate the safety, tolerability and IOP-lowering effects of INS117548 in approximately 60 subjects with early stage glaucoma or ocular hypertension. We expect to have data from both of these glaucoma clinical trials in 2009. Based upon the results of these clinical trials, we may explore the out-licensing of certain rights related to our glaucoma program.

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 that may be 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 $2.1 billion in annual sales in the United States based on data compiled and reported by IMS Health as of December 31, 2008.

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, 2008, 2007 and 2006—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*. We work with Allergan collaboratively on overall product strategy and management in the United States. 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. Allergan also retains the rights relating to promotion of *Elestat* to U.S. prescribers other than ophthalmologists, optometrists and allergists.

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 initial 12-month period immediately following the termination of the agreement, Allergan will be obligated to pay to us 20% of any net sales of *Elestat* in the United States. Allergan will be obligated to pay us 15% of any net sales in the United States in the second 12-month period following termination and 10% of any net sales in the United States in the third, and final, 12-month period following termination of the agreement. 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 if we fail to meet a defined minimum of net sales in any given year, or 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 co-promotion 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 co-promotion 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 and when we receive FDA approval and *Prolacria* is launched, we expect to begin co-promoting 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 co-promotion 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, Taiwan, Korea, Hong Kong and China. In December 2003, at the time we entered into the co-promotion agreement relating to *Elestat*, we amended the joint license, development and marketing agreement to reduce the co-promotion revenue rates that we receive on net sales of *Restasis*.

In December 2008, we amended our agreement with Allergan a second time 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 certain 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 will be responsible for such activities if a product receives regulatory approval in 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 the FDA approval of *AzaSite*. In addition, we are obligated to pay a

20% royalty for the first two years of commercialization and a 25% royalty thereafter on net sales of *AzaSite* in the United States and Canada. We will begin paying a 25% royalty in July 2009. 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 first of which commenced on October 1, 2008.

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.

In addition, 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.

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*) 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.

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. We are 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, 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. Depending on whether all milestones are achieved, we could receive up to an additional $1.75 million, as well as royalties on net sales of DE-089 if it is approved for commercialization 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.

Wisconsin Alumni Research Foundation

In November 2004, we licensed several patents 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 monies 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.

Discontinued Program—Epinastine nasal spray for allergic rhinitis

We previously entered into a development and license agreement, dated February 17, 2006, with Boehringer Ingelheim pursuant to which we were granted certain exclusive rights to develop and market an intranasal dosage form of epinastine in the United States and Canada, for the treatment or prevention of rhinitis. Under the terms of the agreement, we paid Boehringer Ingelheim an upfront license fee of $2.5 million in 2006. On April 23, 2008, we announced that our Phase 3 trial with epinastine nasal spray did not meet its primary endpoint. Based upon the overall data relating to the program and the competitive environment in allergic rhinitis, we decided to discontinue development of epinastine nasal spray. As a result, we terminated our license agreement with Boehringer Ingelheim, effective October 2008. We are no longer responsible for the epinastine nasal spray development program in the United States and Canada and the rights previously granted to us reverted back to Boehringer Ingelheim.

Terminated Agreement—Ophthalmic Research Associates, Inc.

On October 15, 2007, we entered into a clinical service agreement with Ophthalmic Research Associates, Inc., or ORA. During 2008, ORA completed a pilot trial of *Prolacria* under the terms of the agreement using its

proprietary dry eye model (i.e., the controlled adverse environment or dry eye chamber). Following the pilot trial with ORA, we analyzed the overall *Prolacria* clinical trial data, including the pilot trial data, consulted with experts, and decided to design and conduct an environmental trial. We terminated the clinical services agreement with ORA in September 2008.

Research and Development

Since our inception, we have made substantial investments in research and development. During the years ended December 31, 2008, 2007 and 2006, our research and development expenses were $44.6 million, $53.4 million and $42.5 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. Prior to this restructuring, we had a fully integrated research and preclinical organization with expertise in medicinal chemistry, development chemistry, molecular pharmacology, biochemistry, screening and preclinical drug evaluation which conducted discovery and preclinical activities to advance promising compounds to pre-IND status and preclinical studies to support an IND filing.

The progression of product candidates through the various stages of development is overseen by our Portfolio Management Board. When a product candidate is judged as ready for human testing, an IND is filed with the FDA that, in the absence of FDA objections, allows us to embark on human testing in the United States. Other regulatory filings outside of the United States are completed as necessary. 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 are promoting *AzaSite* and *Elestat* in the United States. 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 function 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, federal and state law, such as the Sarbanes-Oxley Act of 2002; U.S. Foreign Corrupt Practices Act of 1977; NASDAQ listing requirements; Financial Industry Regulatory Authority; Securities and Exchange Commission; Food and Drug Administration; United States Department of Health and Human Services; Office of Inspector General; and 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*.

In addition, we have relied 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 *Prolacria* and 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.*"

We are also in discussions with additional third-party manufacturers for the purpose of establishing a secondary source of supply for denufosol. See "Risk Factors—"*The third-party vendor manufacturing denufosol and the API related to Prolacria and Santen's DE-089 does not currently have the capacity to manufacture the projected commercial quantities of API for all three 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.

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 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 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.

Our competitors or potential competitors may have filed for, or have received, United States and foreign patents and may obtain additional patents and proprietary rights relating to compounds, uses and/or processes which may compete with our product candidates. Accordingly, there can be no assurance that our patent applications will result in patents being issued or that, if issued, the claims of the patents will afford protection against competitors with similar technology, nor can we be sure that others will not obtain patents that we would need to license or circumvent in order to practice our inventions.

Competition

Many pharmaceutical and biotechnology companies engage in research and development to commercialize products to treat allergic conjunctivitis, bacterial conjunctivitis, blepharitis, dry eye disease, cystic fibrosis, 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 may compete with our products and product candidates:

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. *Patanol* and *Pataday* currently have the majority of the prescriptions in the allergic conjunctivitis market. Additionally, ISTA Pharmaceuticals, Inc.'s NDA for *Bepreve*™ was accepted for review by the FDA in January 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 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. Additionally, in December 2008, the FDA Dermatologic and Ophthalmic Drugs Advisory Committee voted to recommend approval of Bausch & Lomb's besifloxacin ophthalmic suspension.

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. 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: aztreonam lysine by Gilead Sciences, Inc, and dry powder inhaled mannitol by Pharmaxis.

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. For example, Lantibio, Inc. is developing sodium hyaluronate 0.18% ophthalmic solution (known as

VISMED® in territories in Europe and Asia) for the treatment of dry eye in the United States and submitted an NDA to the FDA in January 2009. Lantibio is partnered with Alcon, Inc. for U.S. commercialization of this product, if approved.

Governmental Regulation

The research, development, testing, manufacture, promotion, marketing and distribution of human therapeutic and diagnostic products are extensively regulated by governmental authorities in the United States and other countries. The FDA regulates drugs and diagnostic 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. The IND process may be costly and substantially delay development of our products. 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 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. A number of legislative and regulatory proposals to change the health care system have been considered in recent years and are still under consideration,

while new proposals are likely under a new Presidential administration. In addition, an increasing emphasis on managed care and government payors in the United States has and will continue to increase pressure on drug pricing. Legislative or regulatory proposals or changes in managed care systems may be announced or adopted that may have an adverse effect on our business and our financial condition, including our profits. The potential for adoption of health care reform proposals on a state-by-state basis could 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 and private insurance plans. These third-party payors frequently require that drug companies give them predetermined discounts from list prices, and they are increasingly challenging the prices for medical products and services. Third-party payors may not consider products we may bring to the market 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 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 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. 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 can be expected to continue to issue guidance and regulations regarding the obligations of Part D sponsors and their subcontractors. 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*.

Each participating drug plan is permitted by regulation to develop and establish its own unique drug formulary that may exclude certain drugs from coverage, impose prior authorization and other coverage restrictions, and negotiate payment levels for drugs which may be lower than reimbursement levels available through private health plans or other payers. Moreover, beneficiary co-insurance requirements could influence which products are recommended by physicians and selected by patients. 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 from the Medicare prescription drug 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 payments may be magnified by private insurers adopting similar lower payment. New federal or state drug payment changes or health care reform in the United States and in foreign countries may be enacted or adopted in the future that could further lower payment for our products.

Employees

As of January 31, 2009, we had approximately 250 full-time and part-time employees, prior to a restructuring which occurred in February 2009, whereby approximately 20 positions were eliminated. 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:

- Continued 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 will require 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.

The manufacture and sale of *Restasis* is protected under a use patent that expires in August 2009 and a formulation patent that expires in May 2014. While a formulation patent may afford certain limited protection, following the expiration of the use patent, a competitor may attempt to gain FDA approval for a cyclosporine product using a different formulation some time after August 2009. 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.

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 attributable to *Elestat* will be minimal.

In December 2003, we entered into an agreement with Allergan to co-promote *Elestat* in the United States. 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 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 initial 12-month period immediately following the termination of the agreement, Allergan will be obligated to pay to us 20% of any net sales of *Elestat* in the United States. Allergan will be obligated to pay us 15% of any net sales in the United States in the second 12-month period following termination and 10% of any net sales in the United States in the third, and final, 12-month period following termination of the agreement.

On September 30, 2008, the USPTO issued a method of treatment patent related to the *Elestat* Patent to an affiliate of Boehringer Ingelheim, the developer of the invention. Notwithstanding the fact that the *Elestat* Patent

was issued by the USPTO, subject to applicable law, competitors are permitted to submit to the FDA an ANDA or a 505(b)(2) application 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 *Elestat* Patent 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). We have been further notified by Allergan that Boehringer Ingelheim has decided not to file infringement lawsuits against the ANDA filers. Boehringer Ingelheim is the owner of the *Elestat* Patent and we do not have a license to the *Elestat* Patent.

We plan to continue co-promoting and receiving co-promotion revenues on *Elestat* sales during the FDA's review period of these ANDAs, which we currently expect to continue beyond 2009. 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*. As a result, we expect to be required to stop the co-promotion of *Elestat* with little, if any, advance notice. Loss of our 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 potential loss of patent exclusivity, as discussed in the previous risk factor, we have the responsibility for promoting and marketing *Elestat* in the United States and paying the associated costs pursuant to our agreement with Allergan. Allergan is responsible for determining the formularies upon which *Elestat* is listed and making the appropriate regulatory and other filings. Our present revenues depend upon and our future revenues will depend, at least in part, upon the continued acceptance of *Elestat* by eye care professionals, allergists and patients. 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.

Under our agreement with Allergan related to our co-promotion of *Elestat,* we are obligated to meet predetermined minimum calendar year net sales target levels through fiscal 2009. To the extent net sales of *Elestat* do not meet the minimum annual net sales requirements, the percentage of net sales of *Elestat* payable to us will be reduced.

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 synthesis 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 both drug substance and finished drug products and 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*. It is our understanding that 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 have relied 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. 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 manufacturing denufosol and the API related to *Prolacria* and Santen's DE-089 does not currently have the capacity to manufacture the projected commercial quantities of API for all three products, if approved.

A single party currently manufactures the clinical supplies of denufosol, and the API for *Prolacria* and Santen's DE-089. Such manufacturer does not presently have capacity to manufacture projected commercial supplies of API for all three of these product candidates at the same time, if necessary. As a result, we are currently in discussions with such manufacturer to further assess its intent to increase capacity and/or to acquire

access to its manufacturing know-how and processes. In addition, we are in discussions with additional third-party manufacturers for the purpose of establishing a secondary source of supply for denufosol.

If a third-party manufacturer is unable to timely produce sufficient commercial quantities of denufosol, or the API for each of DE-089 and *Prolacria*, the launch of such product candidate following approval (if any) may be significantly delayed. Furthermore, insufficient supply of denufosol, or the API for each of DE-089 and *Prolacria*, following any product launch would significantly impact the commercial success of such product(s). A failure to achieve sufficient commercial supply would likely result in a loss of sales in the case of denufosol and a reduction of royalty income associated with each of DE-089 and *Prolacria*.

Risks Related to Product Development

Even if our Trial 03-113 is successful in meeting its primary endpoint, the FDA may not approve our NDA for *Prolacria*.

We have not received marketing approval for any of our internally developed product candidates. We have received two approvable letters from the FDA regarding *Prolacria*. The FDA may not approve the NDA for *Prolacria* and allow the commercialization of the product in the United States.

We have initiated a Phase 3 environmental clinical trial (Trial 03-113) to evaluate the efficacy and safety of *Prolacria* in approximately 450 subjects with dry eye. The FDA indicated, as part of the SPA review process for such trial, that even if the trial is successful, the FDA's review of *Prolacria* will also take into account the robustness of the trial results, that a surrogate endpoint was used, the results from previous *Prolacria* trials and the overall risk/benefit of the product. There can be no guarantee that the FDA would approve *Prolacria* even if such additional clinical trial is successful in meeting its primary endpoint. If additional Phase 3 clinical trials for *Prolacria* are required by the FDA, we may decide not to conduct those clinical trials, which would result in the inability to obtain FDA approval for *Prolacria*.

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 have received two approvable letters from the FDA for *Prolacria*. The FDA has not published guidelines on the approval of a product for the treatment of dry eye disease. Furthermore, to date, only one prescription product, *Restasis*, has been approved by the FDA for the treatment of dry eye disease, and *Restasis* has a different mechanism of action from *Prolacria*. It will be necessary to undertake at least one additional Phase 3 clinical trial in support of our NDA for *Prolacria* and 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 are developing denufosol as an inhaled product designed to enhance the lung's innate mucosal hydration and mucociliary clearance mechanisms by mitigating the underlying ion transport defect in the airways 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 mitigates the underlying ion transport defect in the airways 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, toxicology and carcinogenicity studies. We may later decide to change the focus or timing of a 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 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, 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. We have not yet established a plan to develop a multi-dose formulation. Although our partner, Santen, is developing a multi-dose formulation for use in its licensed territories, a multi-dose formulation has not been developed by our other partner, Allergan, for use in the remainder of the world. In addition, in our current clinical trials, denufosol for the treatment of cystic fibrosis is administered by a standard nebulizer three times-a-day, but clinical data from our TIGER-1 clinical trial indicated that patients in that study administered the drug only 2.7 times-a-day, on average. Patients may prefer a smaller, more portable device or less frequent dose administration. 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. The timing of our Phase 3 program for denufosol for the treatment of cystic fibrosis will be impacted by a number of variables, including clinical development decisions regarding identifying the optimal treatment regimens, patient population, competition for clinical trial participants, approval of other products during our clinical trials, number and length of clinical trials, regulatory requirements of the FDA and/or foreign regulatory authorities, the exclusion criteria for the clinical trials and use of therapies such as hypertonic saline. Our cystic fibrosis clinical trials will present some unique challenges due to the early-intervention approach we are taking with regard to the clinical trials. This approach will require studying mild patients, which are usually younger patients who do not typically participate in clinical trials since new products are generally focused on the sicker patient population and we may have difficulty recruiting such patients for our clinical trials. 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. 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. 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 warning letters, suspension of manufacturing, seizure of product, court-ordered injunction, or voluntary recall of a product.

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 or withdrawal of marketing approval.

In its regulation of advertising, the FDA may issue correspondence to pharmaceutical companies alleging that its advertising or promotional materials are false or misleading. The FDA has the power to impose a wide array of sanctions on companies for such advertising practices, and, if we were to receive correspondence from the FDA alleging these 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.

In addition, in recent years, some alleged violations of FDA requirements regarding off-label promotion of products by manufacturers have been used to support whistleblower and/or government actions under the federal civil False Claims Act, resulting in substantial monetary settlements and the imposition of corporate integrity agreements and deferred prosecution agreements.

Medicare prescription drug coverage legislation and future legislative or regulatory reform of the health care system may affect our or our partner's 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 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. The federal government can be expected to continue to issue guidance and regulations regarding the obligations of Part D sponsors and their subcontractors. 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*.

Each participating drug plan is permitted by regulation to develop and establish its own unique drug formulary that may exclude certain drugs from coverage, impose prior authorization and other coverage restrictions, and negotiate payment levels for drugs which may be lower than reimbursement levels available through private health plans or other payers. Moreover, beneficiary co-insurance requirements could influence which products are recommended by physicians and selected by patients. 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. 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. Also, various legislative proposals have been offered in Congress and in some state legislatures that include major changes in the health care system. These proposals have included price or patient reimbursement constraints on medicines and restrictions on access to certain products. We cannot predict the outcome of such initiatives, and it is difficult to predict the future impact of the broad and expanding legislative and regulatory requirements affecting us.

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.

Failure to adequately ensure compliance with all applicable laws and regulations may adversely affect our business, and we may become subject to investigative or enforcement actions.

There are extensive state, federal, and foreign laws and regulations applicable to pharmaceutical companies engaged in the discovery, development, and commercialization of medicinal products. There are laws and regulations that govern areas including financial controls, clinical trials, testing, manufacturing, labeling, safety, packaging, shipping, distribution, 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.

In recent years, pharmaceutical companies have been the targets of extensive whistleblower actions in which the person bringing the action alleges violations of the 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, 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.

Risks Associated with Our Business and Industry

If we are not able to obtain sufficient additional funding to meet our expanding capital requirements, we may be forced to reduce or eliminate research programs and product candidate development.

We have used substantial amounts of cash to fund our research and development and commercial activities. Our operating expenses were approximately $120.2 million and $114.5 million for the years ended December 31, 2008 and 2007, respectively. Our cash, cash equivalents and investments totaled approximately $73.0 million on December 31, 2008. Based on current operating plans, we expect our cash and investments to provide liquidity through fiscal 2009 and into 2010; however, additional third party funding or milestones will be necessary for our operations to continue throughout 2010 and beyond.

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, 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 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 for *Restasis* and *Elestat* as defined in the co-promotion agreements and as reported to us by Allergan. Accordingly, our co-promotion 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 revenues are currently derived from Allergan's net sales of *Restasis* and *Elestat* as reported to us by Allergan. Management has concluded that our internal control over financial reporting was effective as of the end of the period covered by this report, and these internal controls allow us 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; however, 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 secured 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 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. 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 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 Inspire;
- Breach of our agreements with Allegan; 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 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 $51.6 million and $63.7 million for the years ended December 31, 2008 and 2007, respectively. As of December 31, 2008, our accumulated deficit was approximately $360.5 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, 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 Christy L. Shaffer, Ph.D., 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. We have not entered into agreements with any 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 preclinical and 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 patent 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. Except for patent claims covering new chemical compounds, most 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.

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. Should we choose to do this, as with the above, we may need to make considerable expenditures of money and management time in litigation. Further, we may have to participate in interference proceedings in the 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.

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 regarding the commercialization of *AzaSite*;
- Announcements regarding FDA approval of *Prolacria* or any of our product candidates;
- Announcements made by us concerning results of clinical trials with 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 Pincus is able to exercise substantial control over our business.

Warburg Pincus Private Equity IX, L.P., or Warburg, holds 14,018,600 shares of our common stock which represented approximately 25% of our outstanding common stock as of January 31, 2009. 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, effective July 20, 2007, our Board of Directors elected Jonathan S. Leff as a Class C member of the Board of Directors. 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, 2009, our current 5% and greater stockholders (which includes Warburg) and their affiliates beneficially owned approximately 57% 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 stockholders may conflict with our interests or those of our other stockholders.

Future sales of securities may 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, 2009, there were 56,680,167 shares of common stock outstanding. In addition, we have the ability to sell up to $130 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 under an active shelf registration statement, which we filed with the SEC on March 9, 2007. Up to 15,178,571 shares of our common stock are issued or 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 and our Amended and Restated 2005 Equity Compensation Plan. 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. The remaining shares of common stock outstanding are not registered under the Securities Act of 1933 and may be resold in the public market only if registered or if there is an exemption from registration, such as Rule 144.

If some or all of such shares are sold into the public market over a short period of time, 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 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 Restated Certificate of Incorporation and Amended and Restated Bylaws, 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.

Our employees are covered under Change in Control Severance Benefit Plans which provide severance benefits as of the date on which a change in control occurs. The plans 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 Restated Certificate of Incorporation 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 Restated Certificate of Incorporation 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 Restated Certificate of Incorporation 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.

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 the sale of the Exchangeable Preferred Stock, we agreed to waive Warburg's acquisition of the Exchangeable Preferred Stock 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

Not applicable.

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.

As previously disclosed, a Consolidated Class Action Complaint, or CAC, was filed on March 27, 2006 that asserted claims against Inspire and certain of its present or former senior officers or directors alleging violations of Section 16(b) and 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934, as amended. On June 30, 2006, Inspire and the other defendants moved that the court dismiss the CAC on the grounds that it failed to state

a claim upon which relief could be granted and did not satisfy the pleading requirements under applicable law. 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 CAC with prejudice. On August 24, 2007, the plaintiffs filed an appeal to the United States Court of Appeals for the Fourth Circuit. On December 12, 2008, the Fourth Circuit issued an opinion affirming the judgment of the District Court.

On September 30, 2008, the SEC approved a non-monetary settlement of the previously announced investigation by the SEC staff relating to our disclosures regarding a Phase 3 clinical trial of our dry eye product candidate, *Prolacria*. The SEC also approved settlements with Christy L. Shaffer, our President and Chief Executive Officer, and Mary B. Bennett, who previously served as our Executive Vice President, Operations and Communications.

Under the settlements, we, Dr. Shaffer, and Ms. Bennett each consented to a Securities and Exchange Commission Order Instituting Cease and Desist Proceedings, Making Findings, and Imposing a Cease and Desist Order Pursuant to Section 21C of the Securities Exchange Act of 1934 dated September 30, 2008, or the Order. In particular, we, Dr. Shaffer, and Ms. Bennett consented to a cease and desist order against future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder. We, Dr. Shaffer, and Ms. Bennett did not admit or deny any findings in the Order. The Order does not include any monetary payments or other sanctions. The Order does not affect the current or future employment, or director or officer status, of either Dr. Shaffer or Ms. Bennett.

Item 4. Submission of Matters to a Vote of Security Holders.

Not applicable.

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:

2007	High	Low
First Quarter	$8.29	$5.54
Second Quarter	$8.70	$5.43
Third Quarter	$6.91	$4.65
Fourth Quarter	$7.27	$4.84

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

As of January 31, 2009, there were 55 record stockholders and approximately 4,300 beneficial stockholders of our common stock. On January 31, 2009, the last sale price reported on the Nasdaq Global Market for our common stock was $3.80 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.

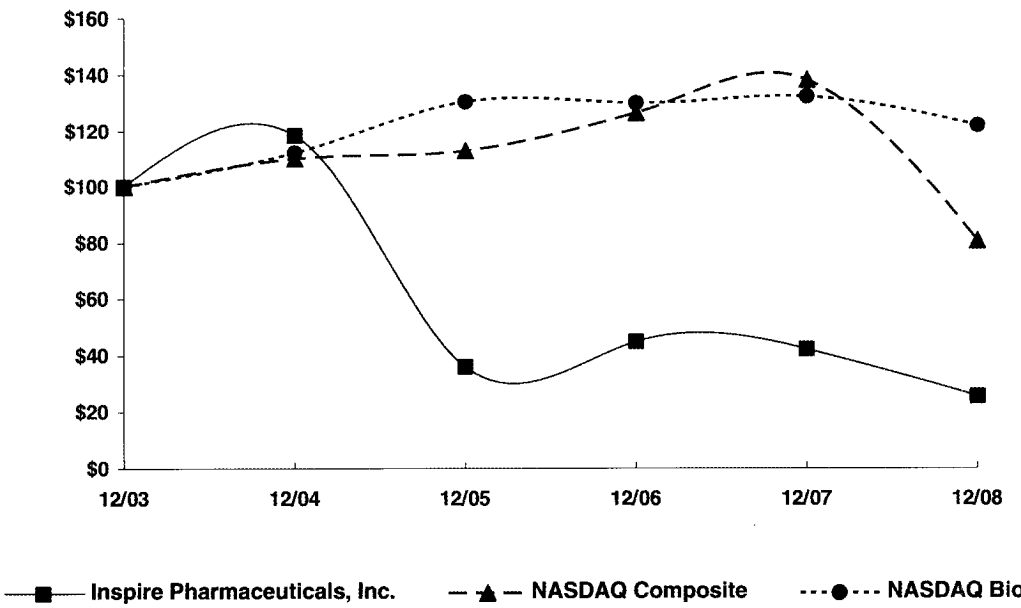
See "Part III—Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" for certain equity compensation plan information.

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, 2003 to December 31, 2008.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

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



* $100 invested on 12/31/03 in stock & index-including reinvestment of dividends.
Fiscal year ending December 31.

	Cumulative Total Returns					
	12/31/03	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08
INSPIRE PHARMACEUTICALS, INC.	$100.00	$118.52	$ 35.90	$ 44.88	$ 42.26	$ 25.44
NASDAQ COMPOSITE	100.00	110.08	112.88	126.51	138.13	80.47
NASDAQ BIOTECHNOLOGY	100.00	112.17	130.53	130.05	132.24	122.10

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, 2008, 2007, 2006, 2005 and 2004 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,				
	2008	2007	2006	2005	2004
Statement of Operations Data:					
Revenue	$ 70,498	$ 48,665	$ 37,059	$ 23,266	$ 11,068
Operating expenses:					
Cost of sales	6,412	1,622	—	—	—
Research and development	44,637	53,391	42,537	23,566	25,698
Selling and marketing	54,568	45,543	25,265	23,223	21,848
General and administrative	14,540	13,986	15,880	12,004	9,041
Total operating expenses	120,157	114,542	83,682	58,793	56,587
Loss from operations	(49,659)	(65,877)	(46,623)	(35,527)	(45,519)
Other income/(expense), net	(1,944)	2,137	4,508	3,680	1,450
Net loss	$ (51,603)	$ (63,740)	$ (42,115)	$ (31,847)	$ (44,069)
Non-cash deemed dividend related to beneficial conversion feature of exchangeable preferred stock	—	(8,285)	—	—	—
Net loss attributable to common stockholders	$ (51,603)	$ (72,025)	$ (42,115)	$ (31,847)	$ (44,069)
Net loss per common share—basic and diluted	$ (0.91)	$ (1.61)	$ (1.00)	$ (0.76)	$ (1.25)
Common shares used in computing weighted average common shares outstanding—basic and diluted	56,609	44,763	42,227	42,101	35,261

	(in thousands)				
	December, 31				
	2008	2007	2006	2005	2004
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 72,966	$139,724	$102,281	$122,323	$156,796
Trade receivables, net	16,544	12,974	8,245	4,898	3,501
Inventories, net	689	1,280	—	—	—
Working capital	52,512	107,651	89,655	99,265	134,559
Total assets	114,224	180,503	116,699	132,446	165,696
Deferred revenue	—	371	—	—	—
Debt obligations, including current portion (1)	43,605	57,701	21,357	1,392	1,881
Total stockholders' equity	44,387	91,693	78,371	118,689	149,598
Shares of common stock outstanding	56,672	56,501	42,238	42,211	41,845

(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 one 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 be able to obtain 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. We launched *AzaSite* in August 2007 and began recording product revenue in the third quarter of 2007. 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 sales of *Restasis*. Our co-promotion 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 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 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 synthesis and manufacturing, preclinical testing 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 basic research activities and clinical trial 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. We have incurred and expect to continue to incur significant costs related to the commercialization of *AzaSite.*

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 *Prolacria* for dry eye and denufosol tetrasodium for cystic fibrosis, which are both in Phase 3 development and *AzaSite* for blepharitis, which is beginning Phase 2 development. We receive revenues 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.

Prior to 2004, we devoted substantially all of our efforts to the discovery and clinical development of our product candidates as well as the establishment of strategic partnerships, and our revenues consisted of payments under our various corporate partnerships established for the development and commercialization of our products, if approved. 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.

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, 2008, we had an accumulated deficit of $360.5 million. Revenue from sales of *AzaSite, Restasis* and *Elestat* did not exceed our total operating expenses in 2008. 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 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 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 rebates and incentives, inventory and manufacturing, taxes, stock-based compensation expense, clinical trial, preclinical/toxicology, research and other service 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 (3) collaborative research agreements in accordance with SEC Staff Accounting Bulletin No. 104, "*Revenue Recognition in Financial Statements,*" or SAB No. 104. SAB No. 104 states that revenue should not be recognized until it is 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. Accruals, or reserves, for estimated rebates, discounts, chargebacks and other sales incentives (collectively, "sales incentives") are recorded in the same period that the related sales are recorded and are recognized as a reduction in sales of *AzaSite*. These sales incentive reserves are recorded in accordance with Emerging Issues Task Force, or EITF, Issue No. 01-9, *"Accounting for Consideration Given by a Vendor to a Customer,"* which states that cash consideration given by a vendor to a customer is presumed to be a reduction of the selling price of the vendor's product or services and therefore should be characterized as a reduction of the revenue recognized in the vendor's income statement. Sales incentive accruals, or reserves, are based on reasonable estimates of the amounts earned or claimed on the sales of *AzaSite*. These estimates take into consideration current contractual and statutory requirements, specific known market events and trends, internal and external historical data and experience, and forecasted customer buying patterns. Amounts accrued or reserved for sales incentives are adjusted for actual results and when trends or significant events indicate that an adjustment is appropriate. As of December 31, 2008 and 2007, we had net reserves of approximately $1.3 million and $235,000, respectively, for sales incentives.

In addition to SAB No. 104, our ability to recognize revenue for sales of *AzaSite* is subject to the requirements of Statement of Financial Accounting Standards, or SFAS, No. 48, *"Revenue Recognition When Right of Return Exists,"* or SFAS No. 48, as issued by the Financial Accounting Standards Board, or FASB. SFAS No. 48 states that revenue from sales transactions where the buyer has the right to return the product will

be recognized at the time of sale only if: (1) the seller's price to the buyer is substantially fixed or determinable at the date of sale; (2) the buyer has paid the seller, or the buyer is obligated to pay the seller and the obligation is not contingent on resale of the product; (3) the buyer's obligation to the seller would not be changed in the event of theft or physical destruction or damage of the product; (4) the buyer acquiring the product for resale has economic substance apart from that provided by the seller; (5) the seller does not have significant obligations for future performance to directly bring about resale of the product by the buyer; and (6) the amount of future returns can be reasonably estimated. Customers are able to return short-dated or expired *AzaSite* that meet the guidelines set forth in our return goods 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 after the expiration date, but may differ from customer to customer, depending on certain factors. In accordance with SFAS No. 48, we estimate the level of sales that will ultimately be returned pursuant to our return policy and record a related reserve at the time of sale. These amounts are deducted from our gross sales of *AzaSite* in determining our net sales. Future estimated returns of *AzaSite* are based primarily on the return data for comparative products and our own historical experience with *AzaSite*. We also consider other factors that could impact sales returns of *AzaSite*. These factors include levels of inventory in the distribution channel, estimated remaining shelf life, price changes of competitive products, and current and projected product demand that could be impacted by introductions of generic products and introductions of competitive new products, among others. As of December 31, 2008 and 2007, we had net reserves of approximately $701,000 and $95,000, respectively, for potential returns of *AzaSite*.

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.

We utilize data from external sources to help us estimate our gross to net sales adjustments as they relate to the sales incentives and 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 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.

Product Co-promotion Revenues

We recognize co-promotion revenue based on net sales for *Restasis* and *Elestat*, 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 sales of *Restasis*. Our co-promotion 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 net sales for both *Restasis* and *Elestat*, reported to us by Allergan, as co-promotion revenue. 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 revenue by estimating the portion of Allergan's 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 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. We achieved our annual 2008 net sales target level during the three-month period ended September 30, 2008. Calendar year 2009 is 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. In each of the years ended December 31, 2008 and 2006, we recognized $1.25 million of collaborative research and development revenue. No collaborative research and development revenue was recognized for the year ended December 31, 2007.

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, 2008 and 2007, we had net reserves of $10,000 and $125,000, respectively, for potential overstocking.

Taxes

We account for uncertain tax positions in accordance with FASB Interpretation No. 48, "*Accounting for Uncertainty in Income Taxes*," an interpretation of FASB Statement No. 109, "*Accounting for Income 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 clinical, preclinical/ toxicology, manufacturing, research 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 SFAS No. 123(R), "*Share-Based Payment,*" 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, 2008, 2007 and 2006

Revenues

Total revenues were approximately $70.5 million for the year ended December 31, 2008, as compared to approximately $48.7 million in 2007 and approximately $37.1 million in 2006. 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.* The increase in 2007 revenues as compared to 2006 was primarily due to increased co-promotion revenue from net sales of *Restasis* and product revenue from net sales of *AzaSite*, which we launched in August 2007. In addition, total revenues for both the 2008 and 2006 periods included the recognition of development milestones of $1.25 million from Santen for its development of diquafosol tetrasodium in accordance with our development, license and supply agreement.

Product Sales, net

Product sales of *AzaSite,* net of rebates and discounts, for the year ended December 31, 2008 were approximately $18.3 million, as compared to approximately $3.1 million in 2007 and none in 2006. *AzaSite* was launched by us in August 2007. For the year ended December 31, 2008 based on prescription data from IMS Health, there were approximately 303,000 prescriptions written for *AzaSite*, representing approximately 2% of all prescriptions in the bacterial conjuctivitis market, defined as both branded and generic single-entity ocular antibiotics. In addition, during 2008 we increased our market share from approximately 1% to 7% in eye care specialists, or Ophthalmologists and Optometrists, representing our primary call audience. In comparison, approximately 30,000 prescriptions were written for *AzaSite* in 2007. 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.

Beginning 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.

In connection with the launch of *AzaSite*, we created a managed markets group to establish relationships with wholesalers, commercial managed care organizations, state Medicaid agencies, and Medicare managed care organizations to secure access and reimbursement for *AzaSite. AzaSite* is now reimbursed, without restrictions, on over 70% of all commercial, Medicare Part D and fee-for-service Medicaid patient lives. For the year ended December 31, 2008, the bacterial conjunctivitis market, in terms of prescriptions, decreased approximately 1%, compared to 2007, based on data as reported by IMS Health.

Product Co-Promotion

Total co-promotion revenue from net sales of *Restasis* and *Elestat* for the year ended December 31, 2008 was approximately $50.9 million, as compared to approximately $45.5 million in 2007, and approximately $35.8 million in 2006.

Co-promotion revenue from net sales of *Restasis* for the year ended December 31, 2008 was approximately $32.8 million, as compared to approximately $24.4 million in 2007 and approximately $15.5 million in 2006. The increase in 2008 co-promotion revenue for *Restasis* of approximately $8.4 million, or 34%, as compared to

2007, was primarily due to increased patient usage of *Restasis* and an increase in prescribers, evidenced by an increase of prescriptions year-over-year, as well as an annual price increase in the first quarter of 2008. The increase in 2007 co-promotion revenue for *Restasis* of approximately $8.9 million, or 57%, as compared to 2006, was primarily due to increased patient usage of *Restasis*, resulting in an increase of prescriptions year-over-year due to selling and promotion efforts, including Direct-To-Consumer (DTC) advertising; an annual price increase in the first quarter of 2007; and the final scheduled increase on the percentage of net sales of *Restasis* to which we were entitled.

All of our revenue from *Restasis* is based on worldwide net sales of *Restasis* according to the terms of our collaborative agreement with Allergan. However, for the years ended December 31, 2008, 2007 and 2006, only approximately 2% of our co-promotion revenue from *Restasis* is derived from sales of *Restasis* outside of the United States. Based on national prescription data as provided by IMS Health, *Restasis* has experienced increased year-over-year prescription volume increases of 10%, 22% and 31% for the 12 months ended December 31, 2008, 2007 and 2006, respectively.

Our entitled percentage of net sales of *Restasis* increased a final time in April 2007. For the year ended December 31, 2008, Allergan recorded approximately $444 million of revenue from net sales of *Restasis,* as compared to approximately $345 million in 2007 and approximately $270 million in 2006. 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 sales of *Restasis* at the rates in effect prior to the December 2008 amendment. In February 2009, Allergan provided 2009 guidance and expects net sales of *Restasis* to be in the range of $490-$510 million.

Co-promotion revenue from net sales of *Elestat* for the year ended December 31, 2008 was approximately $18.1 million, as compared to approximately $21.1 million in 2007, and approximately $20.3 million in 2006. 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. The slight increase in 2007 co-promotion revenue for *Elestat* was primarily due to a reduction in rebates and discounts as a result of changes in *Elestat* coverage under governmental and commercial health plans, combined with a price increase for *Elestat* that became effective during the first quarter of 2007. These factors increased our average price per prescription in 2007 as compared to 2006. These increases in revenue were offset by a decline in market share for *Elestat* during 2007 due to an increasingly competitive market environment as well as an overall decline in the allergic conjunctivitis market in terms of prescriptions.

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. Competition from the introduction of both a once-daily branded product and a generic in 2007 and loss of coverage under state Medicaid plans has caused a decrease in market share for *Elestat.* Based upon national prescription data from IMS Health, for the year ended December 31, 2008, *Elestat* prescriptions represented approximately 7% of the total U.S. allergic conjunctivitis market, as compared to approximately 9% in 2007 and approximately 10% in 2006. Based on current trends in prescriptions for *Elestat,* we expect our 2009 market share to remain relatively constant with 2008. 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 6% and 3% for the years ended December 31, 2008 and 2007, respectively, and increased approximately 5% for the year ended December 31, 2006.

Under our agreement with Allergan related to our co-promotion of *Elestat,* we are obligated to meet predetermined minimum calendar year net sales target levels, which increase annually. We are entitled to an escalating percentage of net sales of *Elestat* based upon predetermined calendar year net sales target levels.

During a fiscal year, we recognize product co-promotion revenue associated with targeted net sales levels for *Elestat* achieved during that time period and defer revenue in excess of the sales level achieved. We achieved the annual 2008 net sales target level for *Elestat* during the three month period ended September 30, 2008. In comparison, we achieved the annual net sales target level for *Elestat* during the three month period ended June 30 for fiscal years 2007 and 2006. Accordingly, we expect that it will take us longer to recognize the full amount of co-promotion revenue associated with net sales of *Elestat* in 2009 as compared to 2008. Under the co-promotion agreement with Allergan, calendar year 2009 is the last year that our co-promotion revenues of *Elestat* are subject to annual minimum target levels.

On September 30, 2008, the USPTO issued a method of treatment patent related to the *Elestat* Patent to an affiliate of Boehringer Ingelheim, the developer of the invention. Notwithstanding the fact that the *Elestat* Patent was issued by the USPTO, subject to applicable law, competitors are permitted to submit to the FDA an ANDA or a 505(b)(2) application 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). We have been further notified by Allergan that Boehringer Ingelheim has decided not to file infringement lawsuits against the ANDA filers. Boehringer Ingelheim is the owner of the *Elestat* Patent and we do not have a license to the *Elestat* 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 initial 12-month period immediately following the termination of the agreement, Allergan will be obligated to pay to us 20% of any net sales of *Elestat* in the United States. Allergan will be obligated to pay us 15% of any net sales in the United States in the second 12-month period following termination and 10% of any net sales in the United States in the third, and final, 12-month period following termination of the agreement. We plan to continue co-promoting and receiving co-promotion revenues on *Elestat* sales during the FDA's review period of these ANDAs, which we currently expect to continue beyond 2009. 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 2007. In March 2006, Santen completed its Phase 2 clinical trial testing of diquafosol tetrasodium, which entitled us to receive a milestone payment of $1.25 million. 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 $6.4 million for the year ended December 31, 2008, as compared to approximately $1.6 million for the year ended December 31, 2007. Since *AzaSite* was launched in August 2007, we had no cost of sales in 2006. Cost of sales reflects a 20% royalty to InSite Vision on net sales of *AzaSite* in accordance with our licensing agreement and a charge to the inventory reserve for potential short-dated product.

Cost of sales expense consists of variable and fixed cost components. Variable cost components include the cost of *AzaSite* inventory sold, changes to our inventory reserve for overstocking or short-dated material, distribution, shipping and logistic service charges from our third-party logistics provider and royalties to InSite Vision on net sales of *AzaSite*. 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. Our royalty rate to InSite Vision on net sales of *AzaSite* will increase from 20% to 25% in July 2009. 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 $44.6 million for the year ended December 31, 2008, as compared to approximately $53.4 million in 2007 and approximately $42.5 million in 2006.

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. The increase in research and development expenses of approximately $10.9 million, or 26%, for the year ended December 31, 2007, as compared to 2006, was primarily due to approximately $14.6 million incurred related to *AzaSite*, which included the one-time $13.0 million upfront licensing fee payment upon the execution of the agreement with InSite Vision in which we acquired the exclusive right to commercialize *AzaSite* in the United States and Canada. Research and development expenses associated with our other product candidates' were approximately $38.8 million for the year ended December 31, 2007 and were primarily associated with advancing our programs for denufosol, epinastine nasal spray, glaucoma and *Prolacria.* 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. 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. Our future research and development expenses will depend on the results and magnitude or scope of our clinical and research 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, 2008, 2007 and 2006 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, 2008	
	2008	%	2007	%	2006	%		%
Denufosol tetrasodium for cystic fibrosis	$18,633	42	$13,599	25	$10,316	24	$ 64,780	21
Prolacria (diquafosol tetrasodium) for dry eye disease	7,632	17	4,181	8	1,431	3	50,951	16
INS115644 and INS117548 for glaucoma and related research and development	5,552	12	5,235	10	3,539	8	14,892	5
Epinastine nasal spray for allergic rhinitis [1]	3,383	8	7,991	15	8,110	19	19,849	6
AzaSite [2]	1,621	4	14,598	27	—	—	16,219	5
Bilastine for seasonal allergic rhinitis [3]	—	—	1,313	3	7,139	17	8,452	3
Other research, preclinical and development costs [4]	7,816	17	6,474	12	12,002	29	137,698	44
Total	$44,637	100	$53,391	100	$42,537	100	$312,841	100

(1) On April 23, 2008, we discontinued the development of epinastine nasal spray. Expense in 2006 includes a $2.5 million upfront licensing fee upon the signing of the license and development agreement with Boehringer Ingelheim.

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

(3) This license agreement was terminated by Inspire in January 2008. Expense in 2006 includes a $7.0 million up-front licensing fee upon the signing of the license agreement with FAES.

(4) 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 prior to January 1, 2006. These unallocated costs include 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.

Selling and Marketing Expenses

Selling and marketing expenses were approximately $54.6 million for the year ended December 31, 2008, as compared to approximately $45.5 million in 2007 and approximately $25.3 million in 2006.

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.

The increase in selling and marketing expenses of approximately $20.3 million, or 80%, for the year ended December 31, 2007, as compared to 2006, resulted from an overall increase in various expenses primarily associated with the launch activities related to *AzaSite*, including the expansion of our sales force and creation of our managed care group, as well as marketing and promotional activities. Additionally, we 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 $14.5 million for the year ended December 31, 2008, as compared to approximately $14.0 million in 2007 and approximately $15.9 million in 2006.

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. Prior year general and administrative expenses reflect a large initial reimbursement of legal fees received from our insurance provider related to our stockholder litigation and SEC investigation. These increases were partially offset by a reduction in consulting fees during 2008.

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*. As a result of this settlement, we do not expect to incur future legal costs related to this investigation.

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. As a result of this dismissal, we do not expect to incur significant future legal costs related to this action.

The decrease in general and administrative expenses of approximately $1.9 million, or 12%, for the year ended December 31, 2007, as compared to 2006, was primarily due to lower legal and administrative expenses as a result of reduced legal defense activities associated with our stockholder litigation and SEC investigation, combined with reimbursement of certain legal costs covered under our insurance policies. Legal fees, excluding amounts reimbursed, were approximately $2.0 million for the year ended December 31, 2007, as compared to approximately $4.1 million in 2006. The decrease in legal costs was partially offset by a general increase in annual salaries, personnel related expenses and stock-based compensation expense.

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.

Other Income (Expense)

For the year ended December 31, 2008, we incurred other expense, net of $1.9 million, as compared to approximately $2.1 million in other income, net in 2007 and approximately $4.5 million other income, net in 2006.

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.

The decrease in other income of approximately $2.4 million, or 53%, for the year ended December 31, 2007, as compared to 2006, was primarily due to an increase in interest expense of approximately $2.8 million, primarily associated with borrowing $20.0 million in December 2006 and additional borrowings 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 *Restasis* and *Elestat*, and product revenue from net sales of *AzaSite*. We do not expect our revenue to exceed our operating expenses in 2009.

At December 31, 2008, we had net working capital of approximately $52.5 million, a decrease of approximately $55.2 million from approximately $107.7 million at December 31, 2007. The decrease in working capital was principally due to the funding of normal operating expenses associated with commercialization

activities and the development of our product candidates, as well as repayment of principal on our term loan facility. Additionally, we have made interest and principal payments on our term loan facility. Our principal sources of liquidity at December 31, 2008 were approximately $58.5 million in cash and cash equivalents, approximately $13.7 million in investments, which are considered available-for-sale, and approximately $16.5 million in trade receivables.

On July 20, 2007, we completed a sale of preferred stock to Warburg Pincus Private Equity IX, L.P. 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. We filed a Form S-3 registration statement to register the shares of common stock, which was declared effective in January 2008.

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 $43.6 million was outstanding as of December 31, 2008. 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 8. "Debt"—to our financial statements for further discussion regarding the term loan facility.

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 and legal 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.

2009 Financial Guidance

Our 2009 financial results will be highly dependant on the amount of revenues derived from *AzaSite* and *Elestat* as a result of our commercial efforts, as well as the level of royalty payments received from Allergan with respect to the commercialization of *Restasis*. Based upon current *AzaSite*, *Restasis* and *Elestat* sales trends, we expect to record 2009 aggregate revenue in the range of $80-$90 million. Total 2009 operating expenses are expected to be in the range of $120-$135 million. 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 $8-$13 million. Total estimated selling and marketing, general and administrative, and research and development expenses are estimated to be in the range of $45-$50 million, $14-$18 million and $50-$60 million, respectively. Included within this operating expense guidance are projected stock-based compensation costs of approximately $5 million.

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 2009 is expected to be in the range of $50-$65 million, which incorporates $18 million of principal repayment on our outstanding debt. Based on current operating plans, we expect our cash and investments to provide liquidity through fiscal 2009 and into 2010; however, additional third party funding or milestones will be necessary for our operations to continue throughout 2010 and beyond. 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 2009 we will need to: (1) successfully increase revenues, (2) obtain additional product candidate approvals, which would trigger milestone payments to us, (3) out-license rights to certain of our product candidates, pursuant to which we would receive income, (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) restructure operations. Additionally, we currently have the ability to sell approximately $130 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, 2008, we were in compliance with all of the covenants under our loan and security agreement and project that we will be throughout 2009. If significant additional liquidity is not generated through the various funding alternatives described above, we may not be in compliance with our covenants in the future.

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, 2008 included operating leases of $3.6 million, long-term borrowings of $43.6 million, interest payments of $4.1 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 $25.4 million as of December 31, 2008, 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 $13.8 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 and in the aggregate total $65.0 million.

The table below reflects contractual and potential obligations as of December 31, 2008, but does not reflect obligations entered into in 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, 2008				
Contractual and Potential Obligations	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Capital Lease Obligations	$ 5	$ 5	$ —	$ —	$ —
Debt Obligations	43,600	18,425	25,175	—	—
Interest on Capital Lease and Debt Obligations	4,144	2,794	1,350	—	—
Operating Lease Obligations [1]	3,620	2,003	1,608	9	—
Purchase Obligations [2]	25,364	21,553	3,811	—	—
Minimum Annual License Payments	55	25	30	—	—
Development Milestone Obligations [3][4]	13,750	—	1,450	6,300	6,000
Minimum Royalties and Sales Milestone Obligations [4]	69,000	5,000	24,000	36,000	4,000
Total	$159,538	$49,805	$57,424	$42,309	$10,000

(1) Includes estimated payments of $1,840 for the cancelable portion of operating leases, primarily our fleet vehicles under a master lease agreement. See Note 13, "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, 2008.

(3) Includes $1.9 million of "other long-term liabilities" as recorded on our Balance Sheet as of December 31, 2008.

(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.

Litigation

As previously disclosed, a Consolidated Class Action Complaint, or CAC, was filed on March 27, 2006 that asserted claims against Inspire and certain of its present or former senior officers or directors alleging violations of Section 16(b) and 20(a) and Rule 10b-5 the Securities Exchange Act of 1934, as amended. On June 30, 2006, Inspire and the other defendants moved that the court dismiss the CAC on the grounds that it failed to state a claim upon which relief could be granted and did not satisfy the pleading requirements under applicable law. 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 CAC with prejudice. On August 24, 2007, the plaintiffs filed an appeal to the United States Court of Appeals for the Fourth Circuit. On December 12, 2008, the Fourth Circuit issued an opinion affirming the judgment of the District Court.

SEC Investigation

As previously disclosed, on September 30, 2008, the SEC approved a non-monetary settlement of the previously announced investigation by the SEC staff relating to our disclosures regarding a Phase 3 clinical trial of our dry eye product candidate, *Prolacria*. The SEC also approved settlements with Christy L. Shaffer, our President and Chief Executive Officer, and Mary B. Bennett, who previously served as our Executive Vice President, Operations and Communications.

Under the settlements, we, Dr. Shaffer, and Ms. Bennett each consented to a Securities and Exchange Commission Order Instituting Cease and Desist Proceedings, Making Findings, and Imposing a Cease and Desist Order Pursuant to Section 21C of the Securities Exchange Act of 1934 dated September 30, 2008, or the Order. In particular, we, Dr. Shaffer, and Ms. Bennett consented to a cease and desist order against future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder. We, Dr. Shaffer, and Ms. Bennett did not admit or deny any findings in the Order. The Order does not include any monetary payments or other sanctions. The Order does not affect the current or future employment, or director or officer status, of either Dr. Shaffer or Ms. Bennett.

Impact of Recently Issued Accounting Pronouncements

In October 2008, the FASB issued FASB Staff Position 157-3 *"Determining the Fair Value of a Financial Asset When the Market for That Asset Is Not Active,"* or FSP SFAS 157-3, which clarifies the application of FASB Statement No. 157, *"Fair Value Measurements,"* or SFAS No. 157, in a market that is not active. FSP SFAS 157-3 was effective immediately and there was no impact on our financial statements upon adoption.

In December 2007, the FASB issued SFAS No. 141(R) *"Business Combinations,"* or SFAS No. 141(R). SFAS No. 141(R) revises previous business combination accounting requirements and applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008, which would impact us for any business combinations completed after January 1, 2009. The effect of SFAS No. 141(R) on our consolidated financial position, results of operations or cash flows will depend on the potential future business combinations entered into by us that will be subject to SFAS No. 141(R).

In November 2007, the EITF of the FASB reached consensus on Issue No. 07-1, *"Accounting for Collaborative Arrangements,"* or EITF Issue No. 07-1. EITF Issue No. 07-1 addresses the issue of how costs incurred and revenue generated on sales to third parties should be reported by participants in a collaborative arrangement in each of their respective income statements. EITF Issue No. 07-1 also provides guidance on how an entity should characterize payments made between participants in a collaborative arrangement in the income statement and what participants should disclose in the notes to the financial statements about collaborative arrangements. EITF Issue No. 07-1 is effective for fiscal years beginning after December 15, 2008 and is to be applied retrospectively to all periods presented for all collaborative arrangements existing as of the effective date. We do not expect the adoption of EITF 07-1 to have a material impact to our financial statements.

In June 2007, the EITF of the FASB reached consensus on Issue No. 07-3, *"Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities,"* or EITF Issue No. 07-3. EITF Issue No. 07-3 addresses the issue of when to record nonrefundable advance payments for goods or services that will be used or rendered for research and development activities as expenses. The EITF has concluded that nonrefundable advance payments for future research and development activities should be deferred and recognized as an expense as the goods are delivered or the related services are performed. EITF Issue No. 07-3 is effective for fiscal years beginning after December 15, 2007. As of January 1, 2008, we have adopted EITF Issue No. 07-3 and there was no material impact to our financial statements.

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, 2008, cash equivalents consisted of $1.5 million in a money market account, $51.1 million in a money market fund and $2.0 million in commercial paper with maturities less than 90 days. Our investment portfolio as of December 31, 2008 consisted solely of corporate notes and bonds and commercial paper 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, 2008, our portfolio of available-for-sale investments consisted of approximately $13.7 million of investments maturing within one year. 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. In 2007, mortgage-backed securities referencing sub-prime consumer mortgages experienced a significant increase in default rates, resulting in devaluation of asset prices and reduction in market liquidity. We reduced our exposure to such additional market risk and associated credit risk by eliminating our investments in mortgage-backed and auction rate securities during 2007. As of December 31, 2008, we do not have any direct investments in auction-rate securities or securities that are collateralized by assets that include mortgages or subprime debt.

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, 2008. 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 investment.

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. We have established policies and procedures for assessing market and foreign exchange risk. As of December 31, 2008, 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, 2008. 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, 2008. The effectiveness of our internal control over financial reporting as of December 31, 2008 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 2009 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 2009 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, 2008.

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	9,714,042	$8.16	2,864,230
Equity compensation plans not approved by security holders	0	0	0
Total	9,714,042	$8.16	2,864,230

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 2009 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 2009 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 2009 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, 2006					
Allowance for rebates, chargebacks and other sales incentives	$ —	$ —	$—	$ —	$ —
Allowance for uncollectible accounts	—	—	—	—	—
Inventory allowance	—	—	—	—	—
Allowance for returns	—	—	—	—	—
Valuation allowance for income taxes	90,831	19,177	—	—	110,008
Year ended December 31, 2007					
Allowance for rebates, chargebacks and other sales incentives	—	366	58	(189)	235
Allowance for uncollectible accounts	—	10	—	—	10
Inventory allowance	—	125	—	—	125
Allowance for returns	—	105	13	(23)	95
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	235	2,887		(1,820)	1,302
Allowance for uncollectible accounts	10	—	—	(3)	7
Inventory allowance	125	105	—	(220)	10
Allowance for returns	95	677		(71)	701
Valuation allowance for income taxes	$133,209	$25,321	—	—	$158,530

(1) Deduction as a result of implementing FASB Interpretation No. 48, "Accounting for Uncertainty in Income Taxes."

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/ CHRISTY L. SHAFFER

Christy L. Shaffer
President & Chief Executive Officer and Director

Date: March 13, 2009

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/ CHRISTY L. SHAFFER **Christy L. Shaffer**	President & Chief Executive Officer (principal executive officer) and Director	March 13, 2009
/s/ THOMAS R. STAAB, II **Thomas R. Staab, II**	Chief Financial Officer & Treasurer (principal financial officer and principal accounting officer)	March 13, 2009
/s/ KENNETH B. LEE, JR. **Kenneth B. Lee, Jr.**	Chairman of the Board of Directors	March 13, 2009
/s/ KIP A. FREY **Kip A. Frey**	Director	March 13, 2009
/s/ ALAN F. HOLMER **Alan F. Holmer**	Director	March 13, 2009
/s/ NANCY J. HUTSON **Nancy J. Hutson**	Director	March 13, 2009
/s/ JONATHAN S. LEFF **Jonathan S. Leff**	Director	March 13, 2009
/s/ RICHARD S. KENT **Richard S. Kent**	Director	March 13, 2009

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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, 2008 and December 31, 2007, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2008 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, 2008, 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.

As discussed in Note 2 and Note 11 to the financial statements, the Company changed the manner in which it accounts for uncertain tax positions in 2007.

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 13, 2009

INSPIRE PHARMACEUTICALS, INC.

BALANCE SHEETS
(in thousands, except per share amounts)

	December 31, 2008	December 31, 2007
Assets		
Current assets:		
Cash and cash equivalents	$ 58,488	$ 101,892
Investments	13,663	28,129
Trade receivables, net	16,544	12,974
Prepaid expenses and other receivables	4,186	4,617
Inventories, net	689	1,280
Other assets	357	614
Total current assets	93,927	149,506
Property and equipment, net	2,925	2,826
Investments	815	9,703
Intangibles, net	16,343	17,937
Other assets	214	531
Total assets	$ 114,224	$ 180,503
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 9,843	$ 13,592
Accrued expenses	13,142	13,795
Deferred revenue	—	371
Short-term debt and capital leases	18,430	14,097
Total current liabilities	41,415	41,855
Long-term debt and capital leases	25,175	43,604
Other long-term liabilities	3,247	3,351
Total liabilities	69,837	88,810
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 1,860 and 1,860 shares authorized, respectively; no shares issued and outstanding	—	—
Common stock, $0.001 par value, 100,000 shares authorized; 56,672 and 56,501 shares issued and outstanding, respectively	57	57
Additional paid-in capital	404,991	400,460
Accumulated other comprehensive income/(loss)	(193)	41
Accumulated deficit	(360,468)	(308,865)
Total stockholders' equity	44,387	91,693
Total liabilities and stockholders' equity	$ 114,224	$ 180,503

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,		
	2008	2007	2006
Revenues:			
Product sales, net	$ 18,349	$ 3,142	$ —
Product co-promotion	50,899	45,523	35,809
Collaborative research and development	1,250	—	1,250
Total revenue	70,498	48,665	37,059
Operating expenses:			
Cost of sales	6,412	1,622	—
Research and development	44,637	53,391	42,537
Selling and marketing	54,568	45,543	25,265
General and administrative	14,540	13,986	15,880
Total operating expenses	120,157	114,542	83,682
Loss from operations	(49,659)	(65,877)	(46,623)
Other income/(expense):			
Interest income	2,642	5,082	4,702
Interest expense	(4,586)	(2,919)	(165)
Loss on investments	—	(26)	(29)
Other income/(expense), net	(1,944)	2,137	4,508
Net loss	$(51,603)	$(63,740)	$(42,115)
Non-cash deemed dividend related to beneficial conversion feature of exchangeable preferred stock	—	(8,285)	—
Net loss attributable to common stockholders	$(51,603)	$(72,025)	$(42,115)
Basic and diluted net loss per common share	$ (0.91)	$ (1.61)	$ (1.00)
Weighted average common shares used in computing basic and diluted net loss per common share	56,609	44,763	42,227

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

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2008	2007	2006
Cash flows from operating activities:			
Net loss	$(51,603)	$(63,740)	$(42,115)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization expense	2,134	1,781	213
Depreciation of property and equipment	939	891	1,277
Loss on disposal of property and equipment	7	7	3
Loss on investments	—	26	29
Stock-based compensation expense	4,443	2,998	1,547
Allowance for doubtful accounts	(3)	10	—
Inventory reserve	105	125	—
Changes in operating assets and liabilities:			
Trade receivables	(3,567)	(4,739)	(3,347)
Prepaid expenses and other receivables	345	(765)	(1,098)
Inventories	486	(1,405)	—
Other assets	(40)	—	10
Accounts payable	(3,675)	7,221	2,837
Accrued expenses and other liabilities	(671)	5,350	1,369
Deferred revenue	(371)	371	—
Net cash used in operating activities	(51,471)	(51,869)	(39,275)
Cash flows from investing activities:			
Purchase of investments	(7,574)	(59,975)	(49,789)
Proceeds from sale of investments	30,694	74,501	55,149
Approval milestone payment	—	(19,000)	—
Restricted cash transfer	—	(100)	—
Purchase of property and equipment	(1,045)	(1,970)	(854)
Proceeds from sale of property and equipment	—	—	1
Net cash provided by/(used in) investing activities	22,075	(6,544)	4,507
Cash flows from financing activities:			
Proceeds from long-term debt	—	40,000	20,000
Proceeds from short-term debt	—	—	781
Proceeds from issuance of exchangeable preferred stock, net	—	73,605	—
Issuance of common stock, net	88	266	75
Debt issuance cost	—	(100)	(100)
Payments on notes payable and capital lease obligations	(14,096)	(3,656)	(816)
Net cash provided by/(used in) financing activities	(14,008)	110,115	19,940
Increase/(decrease) in cash and cash equivalents	(43,404)	51,702	(14,828)
Cash and cash equivalents, beginning of year	101,892	50,190	65,018
Cash and cash equivalents, end of year	$ 58,488	$101,892	$ 50,190
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 4,257	$ 2,255	$ 215
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, 2005	42,211	$ 42	$321,984	$(327)	$(203,010)	$118,689
Issuance of common stock	27	—	75	—	—	75
Unrealized gain on investments	—	—	—	175	—	175
Stock-based compensation	—	—	1,547	—	—	1,547
Net loss	—	—	—	—	(42,115)	(42,115)
Balance at December 31, 2006	42,238	42	323,606	(152)	(245,125)	78,371
Issuance of common stock	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	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

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 through fiscal 2009 and into 2010; however, additional third party funding or milestones will be necessary for its operations to continue throughout 2010 and beyond. 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 2009 it will need to: (1) successfully increase revenues; (2) obtain additional product candidate approvals, which would trigger milestone payments to the Company; (3) out-license rights to certain of its product candidates, pursuant to which the Company would receive income; (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) restructure 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 from sales of *Restasis* and *Elestat* 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, 2008 and 2007, 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.

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. The Company had $615 of restricted deposits recorded as long-term investments as of December 31, 2008 and 2007.

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, 2008 and 2007, the Company had $2,657 and $1,063, respectively, in accumulated amortization related to this milestone.

The carrying value 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, 2008, 2007 and 2006.

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, 2008 and 2007, the Company had $515 and $1,055, 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 (3) collaborative research agreements in accordance with Security and Exchange Commission ("SEC") Staff Accounting Bulletin No. 104, "*Revenue Recognition in Financial Statements,*" ("SAB No. 104"). SAB No. 104 states that revenue should not be recognized until it is 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. Accruals, or reserves, for estimated rebates, discounts, chargebacks and other sales incentives (collectively, "sales incentives") are recorded in the same period that the related sales are recorded and are recognized as a reduction in sales of *AzaSite*. These sales incentive reserves are recorded in accordance with Emerging Issues Task Force ("EITF") Issue No. 01-9, "*Accounting for Consideration Given by a Vendor to a Customer,*" which states that cash consideration given by a vendor to a customer is presumed to be a reduction of the selling price

of the vendor's product or services and therefore should be characterized as a reduction of the revenue recognized in the vendor's income statement. Sales incentive accruals, or reserves, are based on reasonable estimates of the amounts earned or claimed on the sales of *AzaSite*. These estimates take into consideration current contractual and statutory requirements, specific known market events and trends, internal and external historical data and experience, and forecasted customer buying patterns. Amounts accrued or reserved for sales incentives are adjusted for actual results and when trends or significant events indicate that an adjustment is appropriate. As of December 31, 2008 and 2007, the Company had net reserves of approximately $1,302 and $235, respectively, for sales incentives.

In addition to SAB No. 104, the Company's ability to recognize revenue for sales of *AzaSite* is subject to the requirements of Statement of Financial Accounting Standards ("SFAS") No. 48, *"Revenue Recognition When Right of Return Exists"* ("SFAS No. 48"), as issued by the Financial Accounting Standards Board ("FASB"). SFAS No. 48 states that revenue from sales transactions where the buyer has the right to return the product will be recognized at the time of sale only if: (1) the seller's price to the buyer is substantially fixed or determinable at the date of sale; (2) the buyer has paid the seller, or the buyer is obligated to pay the seller and the obligation is not contingent on resale of the product; (3) the buyer's obligation to the seller would not be changed in the event of theft or physical destruction or damage of the product; (4) the buyer acquiring the product for resale has economic substance apart from that provided by the seller; (5) the seller does not have significant obligations for future performance to directly bring about resale of the product by the buyer; and (6) the amount of future returns can be reasonably estimated. Customers are able to return short-dated or expired *AzaSite* that meet the guidelines set forth in the Company's return goods 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 after the expiration date, but may differ from customer to customer, depending on certain factors. In accordance with SFAS No. 48, the Company estimates the level of sales that will ultimately be returned pursuant to its return policy and records a related reserve at the time of sale. These amounts are deducted from the Company's gross sales of *AzaSite* in determining its net sales. Future estimated returns of *AzaSite* are based primarily on the return data for comparative products and the Company's own historical experience with *AzaSite*. The Company also considers other factors that could impact sales returns of *AzaSite*. These factors include levels of inventory in the distribution channel, estimated remaining shelf life, price changes of competitive products, and current and projected product demand that could be impacted by introductions of generic products and introductions of competitive new products, among others. As of December 31, 2008 and 2007, the Company had net reserves of approximately $701 and $95, respectively, for potential returns of *AzaSite*.

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 terms that are customary in the industry.

The Company utilizes data from external sources to help it estimate its gross to net sales adjustments as they relate to the sales incentives and 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 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.

Product Co-promotion Revenues

The Company recognizes co-promotion revenue based on net sales for *Restasis* and *Elestat*, 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 sales of *Restasis*. The Company's co-promotion 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 net sales for both *Restasis* and *Elestat,* reported to Inspire by Allergan, as co-promotion revenue. 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 revenue by estimating the portion of Allergan's 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 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. The Company achieved its annual 2008 net sales target level during the three-month period ended September 30, 2008. Calendar year 2009 is 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. The Company recognized $1,250 of collaborative research and development revenue in each of the years ended December 31, 2008 and 2006. No collaborative research and development revenue was recognized for the year ended December 31, 2007.

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. Effective January 1, 2007, the Company accounts for uncertain tax positions in accordance with FASB Interpretation No. 48, "*Accounting for Uncertainty in Income Taxes,*" an interpretation of SFAS No. 109, "*Accounting for Income 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.

(in thousands, except per share amounts)

Stock-Based Compensation

The Company recognizes stock-based compensation expense in accordance with SFAS No. 123(R), *"Share-Based Payment,"* 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 December 2007, the SEC issued Staff Accounting Bulletin No. 110 ("SAB No. 110") regarding the use of the "simplified" method, as prescribed in Staff Accounting Bulletin No. 107 ("SAB No. 107"), in developing an estimate of expected term of "plain vanilla" share options in accordance with SFAS No. 123(R). Under SAB No. 107, the use of the simplified method was limited only through December 31, 2007. Per SAB No. 110, the staff indicated that it would continue to accept, under certain circumstances, if a company concludes that its historical share option experience does not provide a reasonable basis upon which to estimate expected term, the use of the simplified method beyond December 31, 2007. The Company has utilized the simplified method to estimate expected term for share-based payment awards issued in the years ended December 31, 2008, 2007, and 2006. See Note 10 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 by the weighted average number of common shares outstanding. Diluted net loss per common share is computed by dividing net loss 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, 2008, 2007 and 2006 does not include 183, 457 and 482, respectively, of potential common shares, as their impact would be antidilutive.

Comprehensive Loss

Accumulated other comprehensive income/(loss) is comprised of unrealized gains and losses on marketable securities and is disclosed as a component of stockholders' equity. At December 31, 2008 and 2006, the Company had $193 and $152 of unrealized losses on its investments, respectively. At December 31, 2007, the Company had $41 of unrealized gains on its investments.

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

	2008	2007	2006
Net loss	$(51,603)	$(63,740)	$(42,115)
Adjustment for realized losses in net loss	—	26	29
Change in unrealized gain/(losses) on investments	(234)	167	146
Total comprehensive loss	$(51,837)	$(63,547)	$(41,940)

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 $12,314, $11,541 and $4,433 for the years ended December 31, 2008, 2007 and 2006, 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 each of the years ended December 31, 2008 and 2007. The loss of one or more of these wholesalers as a customer could negatively impact the commercialization of *AzaSite*. All co-promotion revenues recognized and recorded were from one collaborative partner, Allergan. The Company is entitled to receive co-promotion revenue from net sales of *Restasis* and *Elestat* under the terms of its collaborative agreements with Allergan, and accordingly, all trade receivables for these two products are solely due from Allergan. 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 ANDA for a generic version of *Elestat*. *Restasis* is protected under a use patent that expires in August 2009 and a formulation patent that expires in May 2014. While a formulation patent may afford certain limited protection, following the expiration of the use patent, a competitor may attempt to gain FDA approval for a cyclosporine product using a different formulation some time after August 2009. 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, 2008. The Company has no foreign cash or investments and maintains all of its cash deposits in financial institutions in the United States.

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*. 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 October 2008, the FASB issued FASB Staff Position 157-3 *"Determining the Fair Value of a Financial Asset When the Market for That Asset Is Not Active,"* ("FSP SFAS 157-3") which clarifies the application of FASB Statement No. 157, *"Fair Value Measurements,"* ("SFAS No. 157"), in a market that is not active. FSP SFAS 157-3 was effective immediately and there was no impact on the Company's financial statements upon adoption.

In December 2007, the FASB issued SFAS No. 141(R) *"Business Combinations"* ("SFAS No. 141(R)"). SFAS No. 141(R) revises previous business combination accounting requirements and applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008, which would impact the Company for any business combinations completed after January 1, 2009. The effect of SFAS No. 141(R) on the Company's consolidated financial position, results of operations or cash flows will depend on the potential future business combinations entered into by the Company that will be subject to SFAS No. 141(R).

In November 2007, the EITF of the FASB reached consensus on Issue No. 07-1, *"Accounting for Collaborative Arrangements"* ("EITF Issue No. 07-1"). EITF Issue No. 07-1 addresses the issue of how costs incurred and revenue generated on sales to third parties should be reported by participants in a collaborative arrangement in each of their respective income statements. EITF Issue No. 07-1 also provides guidance on how an entity should characterize payments made between participants in a collaborative arrangement in the income statement and what participants should disclose in the notes to the financial statements about collaborative arrangements. EITF Issue No. 07-1 is effective for fiscal years beginning after December 15, 2008 and is to be applied retrospectively to all periods presented for all collaborative arrangements existing as of the effective date. The Company does not expect the adoption of EITF Issue No. 07-1 to have a material impact to its financial statements.

In June 2007, the EITF of the FASB reached consensus on Issue No. 07-3, *"Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities"* ("EITF Issue No. 07-3"). EITF Issue No. 07-3 addresses the issue of when to record nonrefundable advance payments for goods or services that will be used or rendered for research and development activities as expenses. The EITF has concluded that nonrefundable advance payments for future research and development activities should be deferred and recognized as an expense as the goods are delivered or the related services are performed. EITF Issue No. 07-3 is effective for fiscal years beginning after December 15, 2007. As of January 1, 2008, the Company has adopted EITF Issue No. 07-3 and there was no material impact to its financial statements.

(in thousands, except per share amounts)

3. Investments

A summary of the fair market value of investments by classification is as follows:

	December 31,	
	2008	2007
Available-for-sale securities	$13,663	$37,017
Restricted deposits	615	615
Preferred stock	200	200
	$14,478	$37,832

The following is a summary of the Company's marketable debt securities which are classified as available-for-sale:

	December 31, 2008			
	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Corporate bonds and commercial paper	$ 8,858	$5	$(200)	$ 8,663
U.S. Government and agencies	4,998	2	—	5,000
Total	$13,856	$7	$(200)	$13,663

	December 31, 2007			
	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Corporate bonds and commercial paper	$36,982	$63	$(28)	$37,017
Total	$36,982	$63	$(28)	$37,017

Maturities of marketable debt securities at fair market value are as follows:

	December 31,	
	2008	2007
Less than one year	$13,663	$28,129
Greater than one year	—	8,888
	$13,663	$37,017

The following table shows the gross unrealized losses and fair value of the Company's 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:

	December 31, 2008					
	Less than 12 months		12 months or greater		Total	
	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Corporate bonds	$6,140	$(200)	$—	$—	$6,140	$(200)
Total	$6,140	$(200)	$—	$—	$6,140	$(200)

(in thousands, except per share amounts)

	December 31, 2007					
	Less than 12 months		12 months or greater		Total	
	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Corporate bonds	$1,999	$(1)	$5,281	$(27)	$7,279	$(28)
Total	$1,999	$(1)	$5,281	$(27)	$7,279	$(28)

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 unrealized losses on the Company's investments in corporate bonds as of December 31, 2007 were primarily due to an increase in interest rates. 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, 2008. Gross realized losses, including impairments, on the Company's available-for-sale securities were $0, $26 and $29 for the years ended December 31, 2008, 2007 and 2006, respectively.

4. Fair Value Measurements

In September 2006, the FASB issued SFAS No. 157, which establishes a framework for measuring fair value, and expands disclosures about fair value measurements. The statement is effective for financial statements issued for fiscal years beginning after November 15, 2007, and interim periods within that fiscal year. In November 2007, the FASB elected to defer for one year the implementation of SFAS No. 157 for certain non-financial assets and liabilities.

The Company adopted the provisions of SFAS No. 157 effective January 1, 2008. Under SFAS No. 157, 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. SFAS No. 157 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 assumptions about the assumptions market participants would use 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).

The Company's assets recorded at fair value have been categorized based upon a fair value hierarchy in accordance with SFAS No. 157. The adoption of SFAS No. 157 did not have a material impact on the Company's fair value measurements. In accordance with the provisions of FASB Staff Position No. FAS 157-2, "*Effective Date of FASB Statement No. 157*," the Company has elected to defer implementation of SFAS No. 157 as it relates to its non-financial assets and non-financial liabilities that are recognized and disclosed at fair value in the financial statements on a nonrecurring basis until January 1, 2009. The Company is evaluating the impact that SFAS No. 157 will have on its non-financial assets and liabilities, but does not expect a material impact on the fair value measure of its non-financial assets and liabilities.

The Company has not elected the fair value option as permitted under SFAS No. 159, "*The Fair Value Option for Financial Assets and Financial Liabilities—Including an Amendment of FASB Statement No. 115*," for financial assets and liabilities existing at January 1, 2008 that were not already measured at fair value or

(in thousands, except per share amounts)

newly transacted in the year ended December 31, 2008. Any future transacted financial assets or liabilities will be evaluated for the fair value election as prescribed by SFAS No. 159.

The following fair value hierarchy table presents information about the Company's assets measured at fair value on a recurring basis as of December 31, 2008:

	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Total Balance as of December 31, 2008
Cash equivalents	$51,066	$ 1,996	$53,062
Investments:			
Available-for-sale securities	5,000	8,663	13,663
Total	$56,066	$10,659	$66,725

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 a money market fund which is primarily invested in U.S. Treasury securities. Level 1 available-for-sale securities consist of a U.S. Treasury security.

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.

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. 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 consider its investments to be other-than-temporarily impaired at December 31, 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, 2008	December 31, 2007
Finished Goods	$ 47	$ 669
Work-in-Process	160	189
Raw Materials	492	533
Consignment Inventory at Wholesalers	—	14
Total Inventories	$699	$1,405
Less Valuation Reserve	(10)	(125)
Total Inventories, net	$689	$1,280

(in thousands, except per share amounts)

During the years ended December 31, 2008 and 2007, the Company recorded valuation reserves of $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 which resulted in a remaining inventory valuation reserve of approximately $10.

6. Property and Equipment

Property and equipment consist of the following:

	Useful Life (Years)	December 31, 2008	December 31, 2007
Equipment	5	$ 6,228	$ 5,588
Leasehold improvements	Lesser of lease term or 5 years	2,225	2,102
Software	5	1,134	1,010
Furniture and fixtures	7	983	896
Computer hardware	3	979	1,131
		11,549	10,727
Less accumulated depreciation		(8,624)	(7,901)
Property and equipment, net		$ 2,925	$ 2,826

The Company leases certain assets under capital lease agreements. The net book value of assets under capital leases at December 31, 2008 and 2007 was approximately $0 and $98, respectively. Accumulated amortization for assets under capital leases at December 31, 2008 and 2007 was $233 and $2,044, respectively.

7. Accrued Expenses

Accrued expenses are comprised of the following:

	December 31, 2008	December 31, 2007
Compensation and benefits	$ 6,060	$ 6,009
Development costs	3,226	3,867
Allowances for discounts, rebates, chargebacks and returns	2,004	330
Selling and marketing costs	479	1,461
Professional fees	351	436
Accrued interest	293	359
Duties and taxes	168	256
Other	561	1,077
	$13,142	$13,795

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

8. 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

(in thousands, except per share amounts)

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.

An initial term loan advance of $20,000 was made to the Company in December 2006. During 2007, the Company borrowed the remaining $40,000 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 equal to 2% of the principal amount being repaid. Amounts cannot be re-borrowed by the Company once repaid. At December 31, 2008, the Company was in compliance with all of the covenants under the loan and security agreement and projects that it will be throughout 2009. If significant additional liquidity is not generated through various funding alternatives as described in Note 1, the Company may not be in compliance with the covenants in the future.

As of December 31, 2008, the Company had net borrowings of $43,600 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, 2008 is $41,221. 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	
2009	$18,425
2010	19,940
2011	5,235
Total	$43,600

9. Stockholders' Equity

Sales of Common Stock

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 Pincus Private Equity IX, L.P. ("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 EITF 98-5, "*Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios*," and EITF 00-27, "*Application of Issue 98-5 to Certain Convertible Instruments*." 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 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.

10. Stock-Based Compensation

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 Stock 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, 2008, there were 312 and 2,552 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, 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.

Also in July 2006, the Compensation Committee authorized the issuance of restricted stock units to each of the Company's executive officers. The restricted stock units vest 20% annually over five years from the date of grant or earlier upon the event of a change in control. Any restricted stock units that have not vested at the time of termination of service to the Company are forfeited. The restricted stock units do not have voting rights, and the shares underlying the restricted stock units are not considered issued and outstanding until conversion. The total number of restricted stock units granted was 195 and these units will convert into an equivalent number of shares of common stock upon termination of employment with the Company.

Basis for Fair Value Estimate of Share-Based Payments

Prior to fiscal 2007, the Company used a blended volatility calculation utilizing volatility of peer group companies with similar operations and financial structures in addition to the Company's own historical volatility

(in thousands, except per share amounts)

to estimate its future volatility for purposes of valuing the share-based payments granted during the 12 months ended December 31, 2006. In fiscal 2007, the Company began using only its own historical volatility to estimate its future volatility due to the lower expected life associated with the stock option grants with five-year terms that the Company began issuing in the second half of 2006 and the insignificant difference between its own historical volatility and the volatility of the peer group based on the new expected life period. However, actual volatility, and future changes in estimated volatility, may differ substantially from the Company's current estimates.

For options issued under the 1995 Plan prior to fiscal 2007, the Company utilized the historical data available regarding employee and director exercise activity to calculate an expected life of the options. Beginning in fiscal 2007, the Company began granting options with shorter options terms and utilized a simplified method of calculating the expected life of options for grants made to its employees under the 2005 Plan in accordance with the guidance set forth in SAB No. 107 and SAB No. 110, as applicable, due to the lack of adequate historical data with regard to exercise activity on options with these shorter terms. For options granted to directors under the 2005 Plan or the 1995 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,		
	2008	2007	2006
Risk-free interest rate	2.43%	4.43%	4.61%
Dividend yield	0%	0%	0%
Expected volatility	65%	67%	80%
Expected life of options (years)	3.9	3.9	4.4
Weighted average fair value of grants (per option)	$2.01	$3.22	$3.17

(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, 2005	5,557	$ 11.38	6.7	$2,628
Granted	1,481	5.05		
Exercised	(28)	(2.69)		
Forfeited/cancelled/expired	(404)	(12.95)		
Outstanding at December 31, 2006	6,606	$ 9.90	5.7	$5,534
Granted	2,284	6.10		
Exercised	(244)	(1.33)		
Forfeited/cancelled/expired	(378)	(11.81)		
Outstanding at December 31, 2007	8,268	$ 9.01	4.9	$3,721
Granted	1,999	4.01		
Exercised	(171)	(0.52)		
Forfeited/cancelled/expired	(565)	(8.27)		
Outstanding at December 31, 2008	9,531	$ 8.16	4.2	$ 253
Vested and exercisable at December 31, 2008	6,270	$ 9.91	3.9	$ 194

Total intrinsic value of stock options exercised for the years ended December 31, 2008, 2007 and 2006 was $534, $1,211 and $54, respectively. Cash received from stock option exercises for the year ended December 31, 2008 was $88. Due to the Company's net loss position, no windfall tax benefits have been realized during the year ended December 31, 2008. As of December 31, 2008, approximately $7,385 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 value of restricted stock units granted is 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. At the date of grant, the 195 restricted stock units had a total fair value of $811. Additionally, approximately $350 of unrecognized share-based compensation expense related to unvested restricted stock units is expected to be recognized over the next 2.6 years.

Additional information pertaining to the Company's restricted stock units is provided in the table below:

	Year Ended December 31,		
	2008	2007	2006
Outstanding restricted stock units	183	195	195
Vested restricted stock units	78	39	—
Fair value of vested restricted stock units	$324	$162	$—

(in thousands, except per share amounts)

The following table summarizes information concerning options outstanding at December 31, 2008:

	Options Outstanding	Weighted Average Exercise Price (per share)	Weighted Average Remaining Contractual Term (in Years)	Options Exercisable
Exercise Price range (per share):				
$ 0.84 - $ 3.98	1,784	$ 3.64	4.5	471
$ 4.39 - $ 5.25	1,826	4.88	4.3	962
$ 5.27 - $ 6.35	1,806	5.96	4.2	896
$ 6.48 - $ 9.42	1,603	8.33	3.6	1,429
$ 9.435 - $ 16.11	1,661	13.40	3.8	1,661
$ 16.76 - $ 20.30	851	18.80	4.8	851
	9,531	$ 8.16	4.2	6,270

Stock-Based Compensation

For the years ended December 31, 2008, 2007 and 2006, the Company recognized total compensation expense of $4,443, $2,998 and $1,547, respectively.

Total stock-based compensation was allocated as follows:

	Year Ended December 31,		
	2008	2007	2006
Research and development	$1,319	$ 822	$ 576
Selling and marketing	1,402	882	293
General and administrative	1,722	1,294	678
Total stock-based compensation expense	$4,443	$2,998	$1,547

(in thousands, except per share amounts)

11. Income Taxes

The Company had no federal, state or foreign income tax expense for the years ended December 31, 2008, 2007 and 2006.

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

	December 31,	
	2008	2007
Current deferred tax assets:		
Compensation related items	$ 289	$ 302
Accrued expenses and other	427	288
Noncurrent deferred tax assets:		
Accrued expenses and other	820	738
Domestic net operating loss carryforwards	116,945	95,720
Research and development credits	29,000	22,605
Property, equipment and intangible assets	6,693	10,177
Stock-based compensation	3,509	2,597
Contributions	434	369
Investments	413	413
Total deferred tax assets	158,530	133,209
Valuation allowance	(158,530)	(133,209)
Deferred tax assets	$ —	$ —

At December 31, 2008 and 2007, 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 $25,321, $23,201 and $19,177 for the years ended December 31, 2008, 2007 and 2006, respectively. The increase in the valuation allowance of $25,321 during the year ended December 31, 2008 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 2008 and prior years of $1,737 that are unlikely to be realized.

As of December 31, 2008, the Company had federal and state net operating loss carryforwards of $292,576 and $324,274, 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 set to expire in 2009 and 2010 are not expected to be 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, 2008 and 2007, the Company had federal research and development and orphan drug credit carryforwards of $29,000 and $22,605, 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 Interpretation No. 48, "*Accounting for Uncertainty in Income Taxes,*" ("FIN No. 48"). FIN No. 48 prescribes a recognition threshold and a measurement attribute for the financial statement recognition and measurement of tax positions taken or expected

(in thousands, except per share amounts)

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 FIN No. 48, 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 FIN No. 48. In conjunction with the adoption of FIN No. 48, the Company did not recognize any amount for the payment of interest or penalties at January 1, 2007. During 2008 and 2007, 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:

	2008	2007
Balance at January 1	$6,651	$4,000
Additions to current year tax positions	1,689	1,637
Additions to tax positions of prior years	48	1,014
Reductions to tax positions of prior years	—	—
Settlements	—	—
Balance at December 31	$8,388	$6,651

All of the Company's unrecognized tax benefits of $8,388 as of December 31, 2008, 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 2003. However, the net operating loss carryforwards and various research and development credits dating back to 1993 are open to adjustment by the taxing authorities.

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,		
	2008	2007	2006
U.S. Federal tax at statutory rate	$(20,685)	$(21,672)	$(14,319)
State taxes (net of Federal benefit)	(2,140)	(2,810)	(1,875)
Change in valuation reserve	25,321	23,201	19,177
Research and development credit	(6,395)	(1,928)	(5,056)
NOL expiration	(22)	—	—
Reversal of the benefit booked in prior years	29	—	—
Nondeductible expenses due to credits	(3)	301	(13)
Other nondeductible expenses	3,895	2,908	2,086
Provision for income taxes	$ —	$ —	$ —

12. 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*. Inspire works with Allergan collaboratively on overall product strategy and management in the United States. 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. Allergan also retains the rights relating to promotion of *Elestat* to U.S. prescribers other than ophthalmologists, optometrists and allergists.

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 initial 12-month period immediately following the termination of the agreement, Allergan will be obligated to pay to Inspire 20% of any net sales of *Elestat* in the United States. Allergan will be obligated to pay Inspire 15% of any net sales in the United States in the second 12-month period following termination and 10% of any net sales in the United States in the third, and final, 12-month period following termination of the agreement.

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, according to the FDA's website (www.fda.gov). The Company has been further notified by Allergan that Boehringer Ingelheim has decided not to file infringement lawsuits against the ANDA filers.

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 if Inspire fails to meet a defined minimum of net sales in any given year, or 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 co-promotion 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 co-promotion revenue from Allergan on net sales of *Restasis* and *Prolacria*, if any, worldwide, excluding most larger Asian markets. The Company began receiving co-promotion revenue from net sales of *Restasis* in April 2004. This agreement was amended in December 2003, in connection with the execution of the co-promotion agreement for *Elestat* to reduce the co-promotion revenue rates that the Company receives on net sales of *Restasis*. In December 2008, the Company amended its agreement with Allergan a second time 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, 2008 and 2007. 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 will be responsible for such activities if the product receives regulatory approval in 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 is 20% on net sales of *AzaSite* for the first two years of commercialization and 25% thereafter. The Company will begin paying a 25% royalty in July 2009. 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 first of which commenced on October 1, 2008. The Company launched *AzaSite* in August 2007, and began paying royalties to InSite Vision in the fourth quarter of 2007.

The Company and InSite Vision have also entered into a supply agreement for the active pharmaceutical ingredient, azithromycin. Previously, InSite Vision has entered into a third party supply agreement for the production of azithromycin. Under the supply agreement, InSite Vision has agreed to supply Inspire's 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 the Company 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 the Company a specified amount of azithromycin.

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.

(in thousands, except per share amounts)

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 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 monies 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.

During the year ended December 31, 2008, the Company terminated its agreements with FAES Farma, S.A. related to bilastine, Boehringer Ingelheim International GmbH related to epinastine, and Ophthalmic Research Associates related to *Prolacria*. Subsequent to the termination of these agreements, the Company had no further financial commitments.

13. Commitments and Contingencies

Operating Leases

Total rent expense for operating leases during 2008, 2007 and 2006 was $2,098, $1,813 and $1,428, respectively. Future minimum lease payments under non-cancelable operating leases as of December 31, 2008 are as follows:

Year Ending December 31,	Operating Leases
2009	$ 983
2010	714
2011	78
2012	4
Total minimum lease payments	$1,779

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.

Capital Leases

The Company is obligated under master capital lease agreements for furniture, equipment and computers, for which the underlying furniture, equipment and computers serve as collateral. The lease terms under these master lease agreements expire 48 months from the date of inception and have interest rates ranging from 8.2% to 9.6%. The carrying value of the Company's capital lease obligations at December 31, 2008 and 2007 approximate their fair value as the interest rates on these obligations approximate rates available in the financial market at such dates. The Company did not enter into any new capital leases during the years ended December 31, 2008, 2007 and 2006. The Company's remaining capital lease obligation as of December 31, 2008 will be fully paid in the first quarter of 2009.

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 $25,364 as of December 31, 2008. 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 and in the aggregate total $65,000.

Contingencies

As of December 31, 2008, 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 $13,750 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.

Litigation

A Consolidated Class Action Complaint (the "CAC"), was filed on March 27, 2006 that asserted claims against the Company and certain of its present or former senior officers or directors alleging violations of Section 16(b) and 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934, as amended. On June 30, 2006, the Company and the other defendants moved that the court dismiss the CAC on the grounds that it failed to state a claim upon which relief could be granted and did not satisfy the pleading requirements under applicable law. On July 26, 2007, the United States District Court for the Middle District of North Carolina granted the Company's and the other defendants' motion and dismissed the CAC with prejudice. On August 24, 2007, the plaintiffs filed an appeal to the United States Court of Appeals for the Fourth Circuit. On December 12, 2008, the Fourth Circuit issued an opinion affirming the judgment of the District Court.

(in thousands, except per share amounts)

SEC Investigation

On September 30, 2008, the SEC approved a non-monetary settlement of the previously announced investigation by the SEC staff relating to the Company's disclosures regarding a Phase 3 clinical trial of the Company's dry eye product candidate, *Prolacria*. The SEC also approved settlements with Christy L. Shaffer, the Company's President and Chief Executive Officer and Mary B. Bennett, who previously served as the Company's Executive Vice President, Operations and Communications.

Under the settlements, the Company, Dr. Shaffer, and Ms. Bennett each consented to a Securities and Exchange Commission Order Instituting Cease and Desist Proceedings, Making Findings, and Imposing a Cease and Desist Order Pursuant to Section 21C of the Securities Exchange Act of 1934 dated September 30, 2008 (the "Order"). In particular, the Company, Dr. Shaffer, and Ms. Bennett consented to a cease and desist order against future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder. The Company, Dr. Shaffer, and Ms. Bennett did not admit or deny any findings in the Order. The Order does not include any monetary payments or other sanctions. The Order does not affect the current or future employment, or director or officer status, of either Dr. Shaffer or Ms. Bennett.

14. 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 2008, 2007 and 2006, the Company elected a safe harbor contribution at 3.0% of annual compensation. These safe harbor contributions totaled $938, $752 and $601 for the years ended December 31, 2008, 2007 and 2006, respectively.

15. 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 co-promotion revenue for *Restasis* in fiscal years 2008, 2007 and 2006, was derived from product sales in the United States.

	Year ended December 31,		
	2008	2007	2006
Product Sales:			
AzaSite	$18,349	$ 3,142	$ —
Co-Promotion Sales:			
Restasis	32,761	24,442	15,525
Elestat	18,138	21,081	20,284
Total	$69,248	$48,665	$35,809

(in thousands, except per share amounts)

16. Quarterly Financial Data (unaudited)

	2008				
	First	Second	Third	Fourth	Total
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)

	2007				
	First	Second	Third	Fourth	Total
Revenue	$ 7,204	$15,361	$ 12,213	$ 13,887	$ 48,665
Cost of sales	—	—	603	1,019	1,622
Net loss	(26,115)	(5,877)	(13,694)	(18,054)	(63,740)
Non-cash deemed dividend related to beneficial conversion feature of exchangeable preferred stock	—	—	—	(8,285)	(8,285)
Net loss attributable to common stockholders	(26,115)	(5,877)	(13,694)	(26,339)	(72,025)
Net loss per common share—basic and diluted	$ (0.62)	$ (0.14)	$ (0.32)	$ (0.51)	$ (1.61)

17. Subsequent Events

In February 2009, the Company eliminated its early preclinical and molecule discovery activities and refocused its resources on the development of existing later-stage clinical programs and commercially available products. The Company will record a liability for the costs associated with the restructuring in the first quarter of 2009 and expects that all restructuring activities will be completed during the 2009 fiscal year.

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).
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	Registration Rights Agreement, dated July 20, 2007, by and between Inspire Pharmaceuticals, Inc. and Warburg Pincus Private Equity IX, L.P. (Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on July 23, 2007).
4.4	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).
4.5	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).
4.6	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).
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†	Form of Non-statutory Stock Option (Incorporated by reference to Exhibit 10.3 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.4*	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).

Exhibit Number	Description
10.5†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Donald Kellerman dated February 3, 2000 (Incorporated by reference to Exhibit 10.24 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.6†	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).
10.7†	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).
10.8†	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).
10.9*	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).
10.10*	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).
10.11†	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).
10.12†	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).
10.13*	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).
10.14*	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).
10.15†	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).
10.16	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).
10.17	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).
10.18†	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).

Exhibit Number	Description
10.19†	Amended and Restated Director Compensation Policy (Incorporated by reference to Exhibit 10.40 to the Company's Annual Report on Form 10-K filed March 11, 2005).
10.20*	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).
10.21†	Inspire Pharmaceuticals, Inc. Change in Control Severance Benefit Plan (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.22†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Christy L. Shaffer (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.23†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Donald J. Kellerman (Incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.24†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Joseph K. Schachle (Incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.25†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Thomas R. Staab, II (Incorporated by reference to Exhibit 10.7 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.26†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Benjamin R. Yerxa (Incorporated by reference to Exhibit 10.8 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.27†	Agreement regarding change in control, dated as of August 2, 2004, by and between Inspire Pharmaceuticals, Inc. and R. Kim Brazzell (Incorporated by reference to Exhibit 10.9 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.28†	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).
10.29†	Inspire Pharmaceuticals, Inc. 2005 Equity Compensation Plan (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on April 21, 2005).
10.33†	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).
10.31†	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).
10.32†	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).
10.33†	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).
10.34†	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).
10.35†	Agreement regarding change in control, dated as of March 2, 2006, by and between Inspire Pharmaceuticals, Inc. and Joseph M. Spagnardi (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on March 8, 2006).

Exhibit Number	Description
10.36*	Development and License Agreement between Inspire Pharmaceuticals, Inc. and Boehringer Ingelheim International GmbH, effective February 17, 2006 (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed May 10, 2006).
10.37†	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).
10.38	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).
10.39	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).
10.40†	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).
10.41*	License Agreement by and between Inspire Pharmaceuticals, Inc. and FAES Farma, S.A, dated as of October 31, 2006 (Incorporated by reference to Exhibit 10.44 to the Company's Annual Report on Form 10-K filed on March 16, 2007).
10.42	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).
10.43*	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).
10.44*	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).
10.45	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).
10.46	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).
10.47†	Amended and Restated Directors Compensation Policy (Incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on May 10, 2007).
10.48†	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).
10.49†	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).
10.50†	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).

Exhibit Number	Description
10.51	Securities Purchase Agreement, dated July 17, 2007, by and 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 July 23, 2007).
10.52	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).
10.53*	Letter Amendment to License Agreement by and between Inspire Pharmaceuticals, Inc. and FAES Farma, S.A., dated as of June 19, 2007 (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2007).
10.54	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).
10.55†	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).
10.56*	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).
10.57†	Amendment of Agreement, dated September 11, 2007, by and between Inspire Pharmaceuticals, Inc. and R. Kim Brazzell (Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on November 9, 2007).
10.58†	Termination of Agreement, dated September 11, 2007, by and between Inspire Pharmaceuticals, Inc. and Joseph M. Spagnardi (Incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on November 9, 2007).
10.59**	Clinical Services Agreement, dated October 15, 2007, by and between Inspire Pharmaceuticals, Inc. and Ophthalmic Research Associates, Inc. (Incorporated by reference to Exhibit 10.60 to the Company's Annual Report on Form 10-K filed on March 14, 2008).
10.60†	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).
10.61†	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).
10.62	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.
10.63†	Amended and Restated Director Compensation Policy dated March 1, 2009.
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.

Exhibit Number	Description
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.

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* 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 13, 2009 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 13, 2009

Exhibit 31.1

INSPIRE PHARMACEUTICALS, INC.

CERTIFICATIONS

I, Christy L. Shaffer, 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 13, 2009

/s/ CHRISTY L. SHAFFER

Christy L. Shaffer
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 13, 2009

/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, 2008, as filed with the Securities and Exchange Commission (the "Report"), I, Christy L. Shaffer, 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 13, 2009

/s/ CHRISTY L. SHAFFER

Christy L. Shaffer
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, 2008, 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 13, 2009

/s/ THOMAS R. STAAB, II

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

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CORPORATE INFORMATION

CORPORATE OFFICERS

R. KIM BRAZZELL, Ph.D.
Executive Vice President
Head, Ophthalmology Business

JOSEPH K. SCHACHLE
Executive Vice President
Chief, Commercial and Corporate Operations

CHRISTY L. SHAFFER, Ph.D.
President and Chief Executive Officer

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

KIP A. FREY [1] [3]
Partner, Intersouth Partners
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

CHRISTY L. SHAFFER, Ph.D. [4]
President and Chief Executive Officer
Inspire Pharmaceuticals, Inc.

[1] Audit Committee member

[2] Compensation Committee member

[3] Corporate Governance Committee member

[4] Development Committee member

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 Friday, June 5, 2009, at 9:00 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

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.

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Suite 200
Durham, NC 27703
www.inspirepharm.com
919-941-9777
NASDAQ: ISPH