



# **FORM 10-K**

## **INSITE VISION INC - ISV**

**Filed: March 17, 2008 (period: December 31, 2007)**

Annual report which provides a comprehensive overview of the company for the past year

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

**FORM 10-K**

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

For the fiscal year ended December 31, 2007

OR

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

Commission file number: 0-22332

**INSITE VISION INCORPORATED**

(Exact name of registrant as specified in its charter)

**Delaware**

(State or other jurisdiction of  
incorporation or organization)

**94-3015807**

(I.R.S. Employer  
Identification No.)

**965 Atlantic Avenue, Alameda CA**  
(Address of principal executive offices)

**94501**  
(Zip Code)

**(510)-865-8800**

(Registrant's telephone number, including area code)

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

<u>Title of each class</u>	<u>Name of each exchange on which registered</u>
Common Stock, \$0.01 par value per share	American Stock Exchange

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

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

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

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

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

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

Large accelerated filer  Accelerated filer   
Non-accelerated filer  Smaller reporting company

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

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The aggregate market value of registrant's Common Stock, \$0.01 par value, held by non-affiliates of the Registrant as of June 30, 2007 was approximately \$109,145,151 (based upon the closing sale price of the Common Stock on the last business day of the registrant's most recently completed second fiscal quarter). Shares of Common Stock held by each officer and director and by each person who owns 5% or more of the Common Stock have been excluded from such calculation as such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

Number of shares of Common Stock, \$0.01 par value, outstanding as of March 14, 2008: 94,585,449.

### **Documents Incorporated By Reference**

Listed below is the document incorporated by reference and the part of the Form 10-K into which the document is incorporated:

Portions of the Registrant's proxy statement (the "Proxy Statement") to be mailed to stockholders in connection with the solicitations of proxies for the Registrant's 2008 annual meeting of stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein.

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**ANNUAL REPORT ON FORM 10-K  
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2007**

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*Except for the historical information contained herein, the discussion in this Annual Report on Form 10-K contains certain forward-looking statements that involve risks and uncertainties, such as statements of our plans, beliefs, objectives, expectations and intentions. Our actual results could differ materially from those discussed herein. Factors that could cause or contribute to such differences include those discussed below in "Risk Factors," as well as those discussed elsewhere herein. The cautionary statements made in this document should be read as applicable to all related forward-looking statements wherever they appear in this document. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. We undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.*

## **PART I**

### **Item 1. Business**

#### **THE COMPANY**

Historically we have been an ophthalmic product development company focused on ophthalmic pharmaceutical products based on our proprietary DuraSite® drug delivery technology. Beginning in 2007, we have expanded beyond ophthalmic products to other topical anti-infectives, including the treatment of ear infections. Our intent is to continue to solidify our franchise in ocular anti-infective topical therapies as well as extend our anti-infective platform to non-ocular topical products.

Our DuraSite® sustained delivery technology is a proven, patented synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a solution, gel or suspension and can be customized for delivering a wide variety of potential drug candidates. We are currently focusing our research and development and commercial efforts on the following topical anti-infective products that formulate the antibiotic azithromycin with our DuraSite® drug delivery technology.

- AzaSite® (azithromycin ophthalmic solution) 1% (ISV-401), a DuraSite formulation of azithromycin, was developed to serve as a broad spectrum ocular antibiotic; approved by the FDA in April 2007 to treat bacterial conjunctivitis (pink eye); and launched by Inspire Pharmaceuticals in August 2007. The key advantages are a significantly reduced dosing regimen leading to better compliance and outcome, with a broad spectrum antibiotic, and a lowered probability of bacterial resistance based on high tissue concentration.
- AzaSite Plus™ (ISV-502), a DuraSite formulation of azithromycin and a corticosteroid is under development for ocular inflammation and infection, or blepharoconjunctivitis, for which there is no FDA approved indicated treatment; we initiated a pivotal Phase 3 trial in December 2007.
- AzaSite Otic™ (ISV-016), a DuraSite formulation of azithromycin and a corticosteroid, is under development for the treatment of bacterial infections of the middle ear (otitis media); and is in preclinical development.
- AzaSite Xtra™ (ISV-405), a DuraSite formulation with a higher percentage of azithromycin, is in preclinical development for the treatment of ocular infection and is targeted at international markets.

*Business Strategy.* Our business strategy is to in-license promising product candidates and technologies from academic institutions and other companies and apply our formulation expertise to create novel differentiated product opportunities, subsequently conduct preclinical and clinical testing, and partner with pharmaceutical companies in the late stages of clinical trials to manufacture, market and sell our products. For select opportunities, we may manufacture, market or sell our own products.

We have also internally developed DuraSite-based product candidates using either non-proprietary drugs or compounds developed by others for non-ophthalmic indications. Currently we are leveraging our success with the DuraSite-technology product platform to develop additional ocular and non-ocular topical anti-infective products. As with in-licensed product candidates, we either have partnered, or generally plan to partner, with pharmaceutical companies to complete clinical development and commercialization of our own product candidates.

*Corporate Information.* Our principal executive offices are located at 965 Atlantic Avenue, Alameda, California 94501. Our telephone number is (510) 865-8800. We were incorporated in 1986 as a California corporation and reincorporated in Delaware in 1987. We make our periodic and current reports available, free of charge, through our website (<http://www.insitevision.com>) under “Investor Relations - SEC Filings” as soon as reasonably practicable after such material is electronically filed with the Securities and Exchange Commission.

## Recent Event

On February 21, 2008, our wholly owned subsidiary, Azithromycin Royalty Sub LLC, or our subsidiary, closed a private placement of \$60 million in aggregate principal amount of promissory notes, or the Notes, to institutional investors. The Notes are secured by royalties to be paid from sales of AzaSite in the United States and Canada and by a pledge by us of the stock of our subsidiary. All interest and principal payments on the Notes will be made solely from royalties and other payments payable under the license agreement with Inspire Pharmaceuticals, Inc., or Inspire, all of which have been transferred to our subsidiary. The Notes are non-recourse and non-convertible and have not been guaranteed by us. Our subsidiary will receive all royalties on the sales of AzaSite until the Notes have been repaid in full; therefore, future royalties, until the Notes are fully paid, will not be available to fund our operations.

The Notes bear interest at 16% per annum payable quarterly beginning May 15, 2008. AzaSite royalties received for any quarter that exceed the interest payments and expenses due for that quarter, will be applied to the repayment of principal of the Notes until the Notes have been paid in full. Any portion of the principal amount of the Notes not repaid on or before the legal final maturity date of May 15, 2019, will be payable on that date. In addition, the Notes may be redeemed at our option on any quarterly payment date, subject to the payment of a redemption premium if repaid on or before February 15, 2012. After February 15, 2012, the Notes may be redeemed without premium. Once the Notes are repaid in full, our subsidiary will retain all future royalty and other payments due under the license agreement with Inspire.

Net proceeds to us from the financing were slightly over \$50 million after deducting transaction costs and \$5 million placed into an Interest Reserve Account. If the AzaSite royalties received for any quarter is not sufficient to pay all of the interest due on the Notes on or prior to February 15, 2010, the Trustee will withdraw funds equal to such insufficiency from the Interest Reserve Account. Any amount that remains in the Interest Reserve Account after February 15, 2010 will be applied to the repayment of principal of the Notes.

## Ophthalmic Anti-Infective Market

We have concentrated most recently on the need for differentiated topical anti-infectives. In the ocular market we have concentrated on eye and eye-lid infections. Today, eye infections are treated with antibiotics as well as antibiotic/corticosteroid combination products. This ocular anti-infective market represented global sales of \$1.5 billion in 2006 according to Navigant Consulting IMS-based data. The market is comprised of two separate product segments:

- Ocular antibiotic products
- Ocular antibiotic/corticosteroid combination products

Some of these infections are either under-treated or do not have an FDA-approved product specific to their indication. These infections can be both acute and chronic. Our goal is to provide effective and differentiated therapeutics for the treatment of acute and chronic ocular infection and inflammation. There are two general areas where our topical ocular anti-infective products can be applied:

- *Acute bacterial conjunctivitis* (pink eye) is a common condition experienced by most people at some point in their lives, but especially prevalent among children. As it is contagious, immediate treatment is recommended. The conjunctiva is the transparent lining on the inside of the eyelids. In bacterial conjunctivitis, bacteria infects this lining, and the white part of the eye may look pink from the inflammation. AzaSite is targeted at treating this contagious disease with significantly lower dosing and a lowered probability of bacterial resistance due to high tissue concentration.
- *Eye-lid infections.*
  - *Blepharitis* is an inflammation of the eyelids, particularly the eyelid margins where the eyelashes grow. It is a common disorder, particularly among the elderly, that results from a malfunction of the oil glands at the base of the eyelashes. This malfunction can lead to the growth of bacteria, which can irritate and inflame the eyelids. An eyelid with blepharitis may become itchy and appear red and swollen with scaly, greasy debris along the lid margin. Blepharitis can be a chronic condition that is difficult to treat.



- *Blepharoconjunctivitis* occurs when conjunctivitis accompanies blepharitis, as it frequently does. A unilateral or bilateral conjunctivitis that persists for four or more weeks is considered chronic. There is considerable overlap of symptoms of all types of blepharitis. It frequently leads to associated ocular surface inflammation, including conjunctivitis, function tear deficiency, and keratitis, an inflammation of the cornea which can develop into corneal ulcers. Blepharoconjunctivitis is a disease with no approved drug therapy indicated for the relief of its chronic symptoms. The typical treatment is eye hygiene using lid scrubs, topical and/or systemic antibiotics, and topical corticosteroids. Our combination antibiotic/corticosteroid product, AzaSite Plus, is targeted at this unmet need by treating both the infection and inflammation.

## Otic Anti-Infective Market

Direct application of a topical anti-infective to the site of an infection will be an improvement over systemic dosing if an appropriate biocompatible vehicle can deliver high concentrations of drug to infected sites and sustain the release of the antibiotic to minimize dosing frequency. Therefore we are expanding our azithromycin-DuraSite platform outside of ocular anti-infectives to those markets where azithromycin has proven itself as an effective systemic drug agent, but a topical azithromycin format has been unavailable.

For our first opportunity outside of the ocular market space, we are focusing on ear infections. According to Hygea Strategies 2007 IMS-based data, the topical otological drugs category is valued at approximately \$600 million globally, with the U.S. accounting for 67% of this market.

The worldwide otological market is fragmented. Companies engaged in the otic market include Alcon Laboratories, Inc., Daiichi Sankyo Co. Ltd., and Monarch Pharmaceuticals Inc. In the U.S., Alcon's Ciprodex, which requires a total of 56 drops per ear infection therapy, is approximately 9% of the U.S. market and neomycin/steroid combination, which requires approximately 200 drops, is approximately 18%, while in Japan Daiichi Sankyo's Floxin, which requires approximately 100 drops per therapy, is 29% of the market and in Italy the neomycin/steroid combination is more than 60%. Ciprodex and Floxin are not yet widely approved in international markets.

A key area where our azithromycin-DuraSite technology can be applied is for acute *otitis media* with tympanostomy tubes (AOMT). Acute *otitis media* is the most common type of ear infection and is most often seen in infants and children. After multiple recurrent episodes of infection within a year -- or fluid in the middle ear that persists for multiple months -- patients often have tympanostomy tubes temporarily implanted in their eardrums as a method to let air in, allowing fluid to drain more easily down the Eustachian tube. The duration of tube treatment is generally 6-12 months. Patients with these tubes have approximately 1.4 recurrent episodes of infection. In the U.S. 1 in 160 children under the age of 3 have tympanostomy tubes. 1% of all children under the age of 5 have them.

Topical antibiotics are used to treat patients with tubes because the medication can easily make its way to the site of infection. Topical antibiotics are used when a patient with tubes is experiencing drainage from the tube or is experiencing ear pain due to inflammation. Physicians will often prescribe a systemic antibiotic for patients who did not respond to topical treatment alone within 3-5 days. Severe cases are often treated both topically and systemically as a first-line defense. According to a study by Navigant Consulting, physicians feel that a corticosteroid component treats the inflammation associated with more severe symptoms more effectively than do antibiotics alone.

By using both azithromycin for the infection and dexamethasone for inflammation, we are developing AzaSite Otic to reduce the duration required for treatment, reduce the number of required doses and either maintain or increase the effectiveness of the topical treatment, much as we did with AzaSite for bacterial conjunctivitis.

## Products and Product Candidates

The following table summarizes the current status of our principal products and product candidates. A more detailed description of each product and product candidate follows the table.

### Principal Products and Product Candidates Active Programs

Product	Indications	Anticipated Benefits	Status
<b>Topical Anti-infectives</b>			
AzaSite (ISV-401)	Bacterial conjunctivitis (pink eye)	Broad spectrum antibiotic with reduced dosing frequency	*Approved and launched in US *NDS filed in Canada
AzaSite Plus (ISV-502)	Blepharoconjunctivitis	Reduced dosing frequency of a broad spectrum antibiotic combined with an anti-inflammatory corticosteroid	*Pivotal Phase 3 trial initiated
AzaSite Otic (ISV-016)	Ear infections	Reduced dosing frequency of a broad spectrum antibiotic combined with an anti-inflammatory corticosteroid	Preclinical
AzaSite Xtra (ISV-405)	Eye infections	Broad spectrum antibiotic with reduced dosing frequency for use outside of North America	Preclinical

#### The AzaSite Product Family of Topical Anti-infectives

*AzaSite: Launched commercially in the United States by Inspire Pharmaceuticals in August 2007 for Bacterial Conjunctivitis (pink eye)*

We have developed a topical formulation of the antibiotic, azithromycin, to treat bacterial conjunctivitis and other infections of the eye. Bacterial conjunctivitis is a common ocular surface disease characterized by inflammation of the delicate skin and mucosa on the inside of the eyelids. These bacterial infections are contagious and are generally accompanied by irritation, itching, foreign body sensation, watering, mucus discharge and redness. The bacterial form of the disease is generally more common in children than adults.

Azithromycin has a broad spectrum of antibiotic activity and is widely used to treat respiratory and other infections in its oral and parenteral forms. AzaSite is an eye drop of 1% azithromycin formulated to deliver sufficient tissue concentrations over a 7-day dosing using our proprietary DuraSite technology. The eye drop is designed to enable superior bactericidal activity against common ocular pathogens and pseudomonas. We believe the key advantages of AzaSite include its once-a-day dosing after the first two days of treatment and the high and persistent levels of azithromycin achieved in the tissues of the eye resulting in a wide spectrum of activity. Clinical studies have shown that AzaSite is well tolerated and efficacious.

In August 2007, Inspire commercially launched AzaSite (azithromycin ophthalmic solution) 1% in the United States pursuant to their license of AzaSite from InSite and approval from the U.S. Food and Drug Administration, or FDA, in April 2007.

In the United States, the marketing emphasis, through our partner Inspire, will focus on pediatricians, general practitioners, optometrists, and ophthalmologists. Pediatricians and general practice physicians write more than 65% of prescriptions for ophthalmic antibiotics. AzaSite is positioned to compete favorably with the newer 4<sup>th</sup> generation fluoroquinolones for antibacterial coverage. Further, AzaSite possesses the advantage of reduced dosing frequency that we believe may increase patient compliance and reduce the likelihood of the development of bacterial resistance.



### *AzaSite Plus (ISV-502) in Phase 3 Trials for Blepharoconjunctivitis*

Our first expansion of our product candidate AzaSite into a larger franchise is the development of a combination of AzaSite with an anti-inflammatory corticosteroid (dexamethasone) for the treatment of blepharoconjunctivitis, an infection of the eyelid and the conjunctiva and one of the most common eye problems in older adults, as well as other ophthalmic infections. In 2006, we completed our preclinical development of this combination product candidate, filed an Investigational New Drug Application, or IND, with the FDA and conducted a Phase 1 clinical trial.

In February 2007, we announced that the preliminary safety data from our Phase 1 trial indicated that AzaSite Plus was well tolerated. No serious adverse events were reported. Treatment-related ocular adverse events were minimal in frequency and equivalent between the treatment and placebo groups. There were no significant differences in intraocular pressure between the AzaSite Plus group and placebo group after 14 days of treatment.

In the fall of 2007, we conducted a pilot study to evaluate endpoints and time points for use in the Phase 3 trials. There were 32 patients with blepharoconjunctivitis who completed the double-masked and randomized trial and received eye drops two times a day for 14 days. The results led to the selection of endpoints for the Phase 3 trials.

In December 2007, we initiated the first of two pivotal Phase 3 trials to evaluate AzaSite Plus for the treatment of blepharoconjunctivitis. The Phase 3 trials will test a total of approximately 900 patients. The dosing regimen consists of one drop in the eye and one on the eyelid, two times a day for 14 days. There are three treatment arms with the objective that AzaSite Plus will show superiority in treating blepharoconjunctivitis over AzaSite and superiority over dexamethasone. The end points required for product approval include lid margin redness, lid swelling, conjunctival redness, ocular discharge, and discomfort symptoms.

### *AzaSite Otic (ISV-016): Pre-Clinical Development for Ear Infections*

We are in the early stages of developing AzaSite Otic for ear infections. The primary indication is for acute otitis media with tympanostomy tubes (AOMT). AzaSite Otic combines both azithromycin and dexamethasone formulated with DuraSite to provide less frequent dosing while maintaining at least equivalent efficacy.

### *AzaSite Xtra (ISV-405): Pre-clinical Development for Ocular Infections in International Markets*

We are in the early stages of developing AzaSite Xtra which is a product candidate with a higher percentage of azithromycin (2%) as part of the formulation than with AzaSite (1%). AzaSite Xtra is being developed primarily to address markets outside of the United States.

## **DuraSite Sustained Delivery Technology**

At the core of our product development program is our DuraSite drug delivery technology. Our DuraSite sustained delivery technology is a patented synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a solution, gel, or suspension and can be customized for delivering a wide variety of potential drug candidates.

The combination of DuraSite plus proven drug products results in differentiated products that have increased efficacy and improved compliance through reduced dosing frequency that yields better outcomes; lowers the development risk by using the proven DuraSite technology with a proven drug product; and lowers development costs.

*Physical Properties.* DuraSite is composed of a cross linked polyacrylic acid polymer, water and salts. We have developed considerable know-how to formulate it for topical applications that have a range of viscosities and physical forms including gels, suspensions and solutions. The size of the dry polymer particle averages 5 microns. The molecular weight of the polymer exceeds  $3 \times 10^7$  Daltons. Upon the addition of water, DuraSite swells to ~100x its original weight.

The polymer entraps water and the active drug product in a bioadhesive matrix. The viscosity of the matrix is controlled by pH. The bioavailability and release characteristics of the drug can be adjusted by altering the chemical environment. The resulting drug delivery system is bioadhesive, sustained release, and compatible with both water soluble and water insoluble molecules.



*Regulatory Status.* The ingredients in the DuraSite sustained release technology are classified by the FDA as Category 1 GRAS (generally regarded as safe). It has been approved by many pharmacopeias, which helps to facilitate worldwide approvals of drugs that contain it. DuraSite has been used commercially in AquaSite, an ophthalmic product for dry eye syndrome, and in AzaSite, a topical anti-infective product for the treatment of bacterial conjunctivitis.

### **Collaborative, Licensing and Service Agreements**

As part of our business strategy, we have entered into, and will continue to pursue additional licensing agreements, corporate collaborations and service contracts. However, there can be no assurance that we will be able to negotiate acceptable collaborative, licensing or service agreements, or that our existing arrangements will be successful, will be renewed or will not be terminated. Below is a description of certain of our key agreements.

*Shin Poong Pharm Co., Ltd.* In December 2007, we entered into an international licensing and distribution agreement for AzaSite with Shin Poong Pharm, Seoul, South Korea, one of the top ten South Korean pharmaceutical companies. This is the first international agreement for AzaSite outside of North America. Under the terms of the agreement, InSite granted exclusive rights to Shin Poong to commercialize AzaSite for ocular bacterial infection in South Korea. Shin Poong will also be responsible for securing approval of AzaSite in South Korea. In exchange, Shin Poong will pay InSite upfront and regulatory milestone payments as well as double-digit royalties on net sales of AzaSite in South Korea, if approved by regulatory authorities. InSite Vision will be responsible for providing manufactured products to Shin Poong at cost.

*Pfizer Inc. and Pfizer Products, Inc.* In February 2007, we entered into a worldwide, exclusive, royalty-bearing licensing agreement with Pfizer, under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus. Under the Pfizer License, we are required to pay Pfizer a single digit royalty based on net sales of the licensed products and to use reasonable commercial efforts to seek regulatory approval for and market licensed products. We have the right to grant sublicenses, subject to Pfizer's prior approval which shall not be unreasonably withheld.

*Inspire Pharmaceuticals, Inc.* In February 2007, we entered into a license agreement, or the Inspire License, with Inspire under which we licensed to Inspire exclusive development and commercialization rights, under our AzaSite patent rights and certain know-how, for topical anti-infective products containing azithromycin as the sole active ingredient for human ocular or ophthalmic indications in the United States and Canada and their respective territories. The Inspire License also provides for nonexclusive licenses under our DuraSite patent rights, container patent rights, Columbia Laboratories, Inc. polymer technology patent rights and certain know-how in the same field of use as described above. We also granted Inspire an exclusive sublicense under the Pfizer patent rights that we have licensed under the Pfizer License discussed above. Inspire has the right to grant sublicenses under the terms of the Inspire License.

Upon the closing of the Inspire License, Inspire paid us an upfront license fee of \$13 million and paid us an additional \$19 million upon FDA approval in April 2007. Inspire also pays us a royalty on its net sales. The royalty rate is 20% on net sales in the first two years of commercialization and 25% thereafter. Inspire is obligated to pay us royalties under the Inspire License for the longer of (i) eleven years from the launch of the first product (August 13, 2007), and (ii) the period during which a valid claim under a patent licensed from us covers a licensed product. For five years after the first year of commercial sale, Inspire is required to pay us the greater of the royalty discussed above or certain tiered minimum royalties. The royalties discussed above are subject to certain reductions in the event of patent invalidity, third party licenses, generic competition and uncured material breach. Such reductions are cumulative but will in no event fall below a low single digit royalty based on applicable net sales. There are certain permitted offsets against both royalties and minimum royalties which are not subject to a floor amount.

Under the Inspire License, we were responsible for obtaining regulatory approval of AzaSite in the U.S. which occurred in April 2007. We subsequently transferred regulatory documentation regarding AzaSite, including the New Drug Application, to Inspire. We are also responsible for obtaining regulatory approval of AzaSite in Canada. On November 30, 2007, we filed a New Drug Submission (NDS) with Health Canada for AzaSite. Within 25 days after obtaining regulatory approval for Canada, we will be responsible for transferring regulatory documentation regarding AzaSite to Inspire. Thereafter, Inspire will be responsible for all regulatory obligations and strategies relating to the further development and commercialization of products in each country. Inspire will also be responsible for commercialization in both countries.



We are obligated to provide to Inspire certain future developments, including know-how and patent rights, developed up to the effective transfer date of the regulatory materials in the U.S. and Canada that are necessary or useful to develop or commercialize any product for bacterial conjunctivitis in those countries. Such developments will be provided without additional fees but any product that includes such developments will be subject to the same royalty rates described above. For certain further developments after such regulatory transfer date, Inspire has a time-limited exclusive option to license such further developments upon terms and conditions to be separately negotiated.

We also entered into a trademark license agreement with Inspire in February 2007 under which we granted to Inspire an exclusive license to the AzaSite trademark and domain name and a nonexclusive license to the DuraSite trademark in connection with the commercialization of products in the U.S. and Canada under the terms of the Inspire License.

We also entered into a supply agreement, or the Supply Agreement, with Inspire in February 2007 for azithromycin. We had previously entered into a third-party supply agreement for the production of azithromycin. Under the Supply Agreement, we 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 customary termination provisions, such as termination for material breach. Either party may terminate the Supply Agreement upon 180 days notice to the other party. In addition, Inspire may terminate the Supply Agreement if our third party supplier moves the location at which the active ingredient is manufactured. After 2012, the Supply Agreement automatically renews for successive three-year periods unless terminated pursuant to the foregoing termination provisions. If we are in breach of our supply obligations under the Supply Agreement, Inspire is permitted to qualify a second source supplier, at our expense, and obtain the active ingredient from such second source. We are obligated under the Supply Agreement to maintain a minimum quantity of the active ingredient in inventory for Inspire's use in manufacturing the licensed products and to maintain the quality agreement negotiated with the supplier. The Supply Agreement also contains certain provisions regarding the rights and responsibilities of the parties with respect to manufacturing specifications, delivery arrangements, quality assurance, regulatory compliance, product recall, and indemnification, as well as certain other customary matters.

*Catalent Pharma Solutions, formerly Cardinal Health PTS, L.L.C.* In September 2005, we entered into a commercial manufacturing supply agreement with Catalent Pharma Solutions, or Catalent for the manufacture of AzaSite commercial units. The agreement had a term of four years subsequent to the approval by the FDA of Catalent as a manufacturer of AzaSite. Payments under the contract are dependent upon rolling production forecasts we provide to Catalent and are subject to certain minimum purchase commitments which escalate over the term of the contract. The AzaSite NDA and manufacturing responsibilities for AzaSite were transferred to Inspire for manufacturing AzaSite for the U.S. and Canada. We continue to have a relationship with Catalent for the manufacture of AzaSite for international partners as well as for other products in our pipeline.

*Bausch and Lomb Incorporated.* In December 2003, we completed the sale of our drug candidate ISV-403 for the treatment of ocular infections to Bausch & Lomb Incorporated or Bausch & Lomb, pursuant to an ISV-403 Purchase Agreement and a License Agreement, or the License Agreement, and collectively, the Asset Sale.

We are entitled to a single digit royalty on future ISV-403 net product sales, if any, in all licensed countries, ending upon the later of the expiration of the patent rights underlying ISV-403 or ten years from the date of the first ISV-403 product sale by Bausch & Lomb. Bausch & Lomb has assumed all future ISV-403 development and commercialization expenses and is responsible for all development activities.

The License Agreement provides Bausch & Lomb a license under certain of our patents related to our DuraSite delivery system for use with ISV-403 and under other non-patented intellectual property used in ISV-403. The License Agreement provides for Bausch & Lomb to complete development of the SS734 fluoroquinolone products that combine certain compounds we licensed from SSP with the DuraSite delivery system and to commercialize any such products. The patent license is exclusive in the particular field of developing, testing, manufacturing, obtaining regulatory approval of, marketing, selling and otherwise disposing of such products. The license of non-patented intellectual property granted to Bausch & Lomb is nonexclusive.

In connection with the Asset Sale, we also assigned to Bausch & Lomb an agreement between SSP and us under which we were licensed to commercialize SSP's SS734 fluoroquinolone. Because that agreement also included a license from us to SSP of certain patents relating to DuraSite that we did not sell to Bausch & Lomb, the assignment of the agreement to Bausch & Lomb excluded the assignment of our obligations and rights as the licensor of such patents. Instead, we entered into a new license agreement with SSP reflecting our original rights and obligations as the licensor of the DuraSite patents to SSP.

*Other.* As part of our basic strategy, we continually pursue agreements with other companies, universities and research institutions concerning additional therapeutic agents and drug delivery technologies to complement and expand our family of proprietary ophthalmic products as well as collaborative agreements for the further development and marketing of our current products and product candidates. We intend to continue exploring licensing and collaborative opportunities, although there is no certainty that we can successfully enter into, or maintain, any such agreements.

## **Patents and Proprietary Rights**

Patents and other proprietary rights are important to our business. Our policy is to file patent applications seeking to protect technology, inventions and improvements to our inventions that we consider valuable. Additionally, we assist University of California Regents in filing patent applications seeking to protect inventions that are the subject of our agreements with that institution. We also rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. Our DuraSite drug delivery products are made under patents and applications, and we have filed a number of patent applications in the United States relating to our DuraSite technology with delivery tips and drug compounds. Of these applications, seven U.S. patents have been issued. Of the patent applications we have licensed from the UC Regents, twelve U.S. patents have been issued. We have four U.S. patents on our retinal drug delivery device that have been issued. Three U.S. patents have been issued related to our antibiotic programs with four applications pending. Several other patent applications by us and by the UC Regents, relating to the foregoing and other aspects of our business and potential business are also pending. Foreign counterparts of our patents as well as those we have licensed from others have been filed in many countries.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued. Consequently, we do not know whether any of our pending patent applications will result in the issuance of patents or if any of our patents will provide significant proprietary protection. Since patent applications are maintained in secrecy until they are published, we cannot be certain that we or any licensor was the first to file patent applications for such inventions or that patents issued to our competitors will not block or limit our ability to exploit our technology. Moreover, we might have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention, which could result in substantial cost to us, even if the eventual outcome were favorable. There can be no assurance that our patents will be held valid or enforceable by a court or that a competitor's technology or product would be found to infringe such patents.

A number of pharmaceutical companies and research and academic institutions have developed technologies, filed patent applications or received patents on various technologies that may be related to our business. Some of these technologies, applications or patents may conflict with our technologies or patent applications. This conflict could limit the scope of the patents, if any, that we may be able to obtain or result in the denial of our patent applications. In addition, if patents that cover our activities have been or are issued to other companies, there can be no assurance that we would be able to obtain licenses to these patents, at all, or at a reasonable cost, or be able to develop or obtain alternative technology. If we do not obtain such licenses, we could encounter delays in or be precluded altogether from introducing products to the market.

In addition to patent protection, we also rely upon trade secret protection for our confidential and proprietary information. There can be no assurance that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets, that such trade secrets will not be disclosed or that we can effectively protect our rights to unpatented trade secrets.

We believe our drug delivery technology may expand the ophthalmic pharmaceutical market by permitting the novel use of drugs for ophthalmic indications that are currently used or being developed for non-ophthalmic indications. However, we may be required to obtain licenses from third parties that have rights to these compounds in order to conduct research, to develop or to market products that contain such compounds. There can be no assurance that such licenses will be available on commercially reasonable terms, if at

all.

## Research and Development

On December 31, 2007, our research and development staff numbered 32 people, of whom 6 have Ph.D.s. Our research and development expenses for the years ended December 31, 2007, 2006 and 2005 were:

### R&D Cost by Program (in millions)

<b>Program</b>	<b>2007</b>	<b>2006</b>	<b>2005</b>
AzaSite	\$ 2.7	\$ 6.1	\$ 10.4
AzaSite Plus	6.0	2.7	0.1
AzaSite Otic	1.3	-	-
AzaSite Xtra	0.4	-	-
Other	-	0.1	0.2
Total	<u>\$ 10.4</u>	<u>\$ 8.9</u>	<u>\$ 10.7</u>

In 2007, our AzaSite program activities included producing registration batches at our contract manufacturing site and assembling and filing the application for regulatory approval in Canada. Our activities related to the AzaSite Plus program focused on the completion of preclinical studies to support Phase 3 clinical trials, the completion and data analysis of a Phase 1 clinical trial, conduct of a pilot study and the initiation of a Phase 3 clinical trial. Our activities related to the AzaSite Otic program mainly consisted of preclinical testing to support filing of an IND. Our AzaSite Xtra activities mainly related to preclinical experiments.

In 2006, our AzaSite activities mainly related to the completion of the Phase 3 clinical trials and compilation and filing of an NDA in the United States. Our AzaSite Plus activities mainly focused on preclinical testing, preparation of an IND and initiation of Phase 1 clinical trials.

In 2005, our AzaSite activities were mainly focused on the conduct of our Phase 3 clinical trials and preparation of other portions of the NDA we filed in 2006 after the completion of the trials.

Although the majority of our personnel were focused on our AzaSite and AzaSite Plus programs in 2007, due to our limited personnel and the number of projects that we are developing including our AzaSite Otic program, our personnel are involved in a number of projects at the same time. Accordingly, the majority of our R&D expenses are not linked to a specific project but are allocated across projects, based on personnel time expended on each project. Accordingly, the allocated costs may not reflect the actual costs of each project.

## Manufacturing

We have no experience or facilities for the manufacture of products for commercial purposes and we currently have no intention of developing such experience or building such facilities. We have a pilot facility, licensed by the State of California, to produce potential products for Phase 1 and some of our Phase 2 clinical trials. However, we rely on third parties for supplies and materials necessary for our Phase 3 clinical trials and commercial needs. If we should encounter delays or difficulties in establishing and maintaining our relationship with qualified manufacturers to produce, package and distribute our finished products, then clinical trials, regulatory filings, market introduction and subsequent sales of such products would be adversely affected.

We have entered into a licensing agreement with Inspire under which they are responsible for the manufacture of AzaSite for the United States and Canada. The AzaSite NDA was transferred to Inspire and manufacturing responsibilities for AzaSite were transferred to Inspire for the U.S. and Canada. We have a relationship with Catalent for the manufacture of AzaSite for international partners as well as for other products in our pipeline.

## Marketing and Sales

The cost to develop and maintain a marketing organization and sales force is significant and would result in the reallocation of resources needed for the development of our product candidates. We do not currently plan on establishing a dedicated sales force or a marketing organization for our AzaSite, AzaSite Plus or other product candidates.

We have entered into corporate collaborations, and we plan to enter into additional collaborations with one or more additional pharmaceutical companies, to market our products. We may not be able to conclude or maintain such arrangements on acceptable terms, if at all.

Our current active collaborators include:

*Shin Poong Pharm Co., Ltd.* In December 2007, we entered into an international licensing and distribution agreement for AzaSite with Shin Poong Pharm, Seoul, South Korea, one of the top ten South Korean pharmaceutical companies. This is the first international agreement for AzaSite outside of North America. Under the terms of the agreement, InSite grants exclusive rights to Shin Poong to commercialize AzaSite for ocular bacterial infection in South Korea. Shin Poong will also be responsible for securing approval of AzaSite in South Korea. In exchange, Shin Poong will pay InSite upfront and regulatory milestone payments as well as a double-digit royalty on net sales of AzaSite in South Korea, if approved by regulatory authorities. InSite Vision will be responsible for providing manufactured products.

*Inspire.* In February 2007, we entered into an exclusive agreement with Inspire under which Inspire obtained the right to exclusively market AzaSite in the United States and Canada. We received a licensing fee, a milestone payment when AzaSite was approved by the FDA and received the first royalty payment based on net sales of the product in the third quarter 2007.

*Bausch & Lomb.* In December 2003, we sold our ISV-403 product candidate to Bausch & Lomb. Bausch & Lomb has the exclusive marketing rights for the world except for Japan, which were retained by SSP, and shared rights in the rest of Asia with SSP. Bausch & Lomb has also assumed the development and manufacturing responsibilities for the ISV-403 formulation for their sales and distribution and we are entitled to royalties based on net sales of the product, if any.

## Competition

The pharmaceutical industry is highly competitive and requires an ongoing commitment to the pursuit of technological innovation. Such commitment requires significant investment in the resources necessary to discover, develop, test and obtain regulatory approvals for products. It also involves the need to effectively commercialize, market and promote approved products, including communicating the effectiveness, safety and value of products to customers and medical professionals.

The global ophthalmic market will become even more competitive going forward as the prevalence of eye disease increases, which will lead to increased demand for new and novel ophthalmic products. The market segments that treat diseases and conditions of the eye are subject to ongoing technological change and evolution.

Many companies are engaged in activities similar to our own. Typically, these companies have substantially greater financial, technical, marketing and human resources available to them, which may allow them to succeed in developing technologies and products that are more effective, safer, and receive greater market acceptance than the therapies that we are developing or have developed. These competitors may also succeed in obtaining cost advantages or intellectual property rights that would limit our ability to develop and commercialize our product opportunities, in addition to obtaining a more timely and effective regulatory approval for the commercialization of their products in comparison to our products.

The global ophthalmic pharmaceutical market is currently dominated by a number of large and well-established companies, including Alcon Laboratories, Inc., Allergan, Inc., Bausch & Lomb, Novartis Ophthalmics, Johnson & Johnson, Merck & Co., and Pfizer Inc. While there are many other large- and medium-sized companies participating in the ophthalmic market, it continues to be very difficult for smaller companies such as our own to successfully develop and market products without entering into effective collaborations with our direct competitors.

Certain segments of the greater ophthalmic market, such as those for glaucoma, anti-infective, and anti-inflammatory agents, already have well-established competing products currently available and also many in development by prominent competitors. New products must exhibit improved efficacy and safety profiles, be supported by strong marketing and sales initiatives, and have the support of industry thought leaders in order to penetrate these competitive mature markets.

The worldwide otological market is fragmented. Companies engaged in the otic market include Alcon, Daiichi Sankyo, and Monarch. In the U.S., Alcon's Ciprodex, which requires a total of 56 drops per therapy, is approximately 9% of the U.S. market and neomycin/steroid combination, which requires approximately 200 drops, is approximately 18%, while in Japan Daiichi Sankyo's Floxin, which requires approximately 100 drops per therapy, is 29% of the market and in Italy the neomycin/steroid combination is more than 60%. Ciprodex and Floxin are not yet widely approved in international markets.

In summary, our competitive position will depend on our ability to develop enhanced and innovative products, maintain a proprietary position in our technology, obtain required government approvals for our products on a timely basis, attract and retain key personnel, and enter into effective collaborations for the manufacture, commercial marketing and distribution of our products in key worldwide markets.

### **Government Regulation**

The manufacturing and marketing of our products and our research and development activities are subject to regulation by numerous governmental authorities in the United States and other countries. In the United States, drugs are subject to rigorous FDA regulation. The Federal Food, Drug and Cosmetic Act and regulations promulgated there-under govern the testing, manufacture, labeling, storage, record keeping, approval, advertising and promotion in the United States of our products. In addition to FDA regulations, we are also subject to other federal and state regulations such as the Occupational Safety and Health Act and the Environmental Protection Act. Product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources.

The steps required before a pharmaceutical agent may be marketed in the United States include:

- preclinical laboratory and animal tests;
- submission to the FDA of an IND;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug;
- the submission of an NDA or Biological License Application, or BLA to the FDA; and
- the FDA approval of the NDA or BLA, prior to any commercial sale or shipment of the drug.

In addition to obtaining FDA approval for each product, each domestic drug manufacturer and facility must be registered with, and approved by, the FDA. Drug product manufacturing establishments located in California also must be licensed by the State of California in compliance with separate regulatory requirements.

Preclinical tests include laboratory evaluation of product chemistry and animal studies to assess the potential safety and efficacy of the product and its formulation. The results of the preclinical tests are submitted to the FDA as part of an IND and, unless the FDA objects, the IND will become effective 30 days following its receipt by the FDA.

Clinical trials involve the administration of the drug to healthy volunteers or to patients under the supervision of a qualified principal investigator. Clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor safety, and the efficacy criteria to be evaluated. Before any clinical trial can commence, each protocol is submitted to the FDA as part of the IND. Each clinical study is conducted under the auspices of an independent Institutional Review Board that considers, among other things, ethical factors and the rights, welfare and safety of human subjects.

Clinical trials are typically conducted in three sequential phases, but the phases may involve multiple studies and may overlap. In Phase 1, the initial introduction of the drug into human subjects, the drug is tested for safety (adverse effects), dosage tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase 2 involves studies in a limited patient population to (i) determine the efficacy of the drug for specific targeted indications, (ii) determine dosage tolerance and optimal dosage and (iii) identify possible adverse effects and safety risks. When a compound is found to be effective and to have an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to further evaluate clinical efficacy and to further test for safety within an expanded patient population at multiple clinical study sites. The FDA reviews both the clinical plans and the results of the trials and may discontinue the trials at any time if there are significant safety issues.

The results of the preclinical studies and clinical studies are submitted to the FDA in the form of an NDA or BLA for marketing approval. The testing and approval process requires substantial time and effort and there can be no assurance that any approval will be granted on a timely basis, if at all. Additional animal studies or clinical trials may be requested during the FDA review period and may delay marketing approval. After FDA approval for the initial indications, further clinical trials are necessary to gain approval for the use of the product for additional indications. The FDA may also require post-marketing testing to monitor for adverse effects, which can involve significant expense.

Among the conditions for manufacture of clinical drug supplies and for NDA or BLA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to current Good Manufacturing Practice, or cGMP. Prior to approval, manufacturing facilities are subject to FDA and/or other regulatory agency inspection to ensure compliance with cGMP. Manufacturing facilities are subject to periodic regulatory inspection to ensure ongoing compliance.

For marketing outside the United States, we or our licensees are also subject to foreign regulatory requirements governing human clinical trials and marketing approval for drugs. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to country and in some cases are even more rigorous than in the United States

## Scientific and Business Advisors

We have access to a number of academic and industry advisors with expertise in clinical ophthalmology and pharmaceutical development, marketing and sales. Our advisors meet with our management and key scientific employees on an ad hoc basis to provide advice in their respective areas of expertise and further assist us by periodically reviewing with management our preclinical, clinical and marketing activities. We plan to make arrangements with other individuals to join as advisors as appropriate. Although we expect to receive guidance from our advisors, all of our advisors are employed on a full-time basis by other entities, or are primarily engaged in outside business activities, and may have other commitments to, or consulting or advisory contracts with, other entities that may conflict or compete with their obligations to us.

Our advisors are as follows:

<u>Name</u>	<u>Position</u>
Mark Abelson, M.D.	Associate Clinical Professor of Ophthalmology, Department of Ophthalmology, Harvard Medical School
Chandler R. Dawson, M.D.	Emeritus Professor, Department of Ophthalmology, University of California, San Francisco
Eric D. Donnenfeld, M.D.	Founding partner of Ophthalmic Consultants of Long Island and Connecticut; Co-Chairman of Cornea and External Disease at Nassau University Medical Center and Surgical Director of the Lions Eye Bank for Long Island.
Syd Gilman, Ph.D.	Partner, Trident Rx Consultant Service
Edward J. Holland, M.D.	Director, Cornea Services at the Cincinnati Eye Institute and Professor of Ophthalmology at the University of Cincinnati; Member of the Board of Trustees for the American Academy of Ophthalmology.
Ping H. Hsu, Ph.D.	Consultant, Biostatistics
David G. Hwang, M.D.	Professor of Clinical Ophthalmology, Co-Director, Cornea and Refractive Surgery Service, University of California, San Francisco School of Medicine
Henrick K. Kulmala, Ph.D.	Consultant, Pharmaceutical Development
Michael Marmor, M.D.	Professor, Department of Ophthalmology, Stanford University School of Medicine
Peter Roland, M.D.	Professor and Chairman, Otolaryngology-Head and Neck Surgery, Professor Neurological Surgery, Chief of Pediatric Otolaryngology, UT Southwestern Medical Center
James G. Shook, Ph.D.	President, Jim Shook Research, Inc.
Kerry D. Solomon, M.D.	Professor of Ophthalmology at the Medical University of South Carolina (MUSC); at MUSC: Director of the Cataract, Refractive and Cornea Services at Storm Eye Institute; Medical Director of the Magill Laser Center for Vision Correction; and Director of the Magill Research Center

## Employees

As of December 31, 2007, we had 45 employees, 43 of whom were full time. None of our employees is covered by a collective bargaining agreement. We believe we have good employee relations. We also utilize independent consultants to provide services in certain areas of our scientific and business operations.



## Item 1A. Risk Factors

***It is difficult to evaluate our business because we are in an early stage of development and our technology is untested and successful development of pharmaceutical products is highly uncertain and requires significant expenditures and time***

We are in the early stages of developing our business, particularly with respect to commercializing our products. We received regulatory approval for AzaSite in April 2007 and commercial sales of AzaSite began in the third quarter of 2007. Before regulatory authorities grant us marketing approval for additional products, we need to conduct significant additional research and development and preclinical and clinical testing and submit an NDA. Successful development of pharmaceutical products is highly uncertain. Products that appear promising in research or development, including AzaSite Plus, may be delayed or fail to reach later stages of development or the market for several reasons, including:

- preclinical tests may show the product to be toxic or lack efficacy in animal models;
- failure to receive the necessary U.S. and international regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by slow enrollment in clinical studies; extended length of time to achieve study endpoints; additional time requirements for data analysis or BLA or NDA preparation; discussions with the United States (U.S.) Food and Drug Administration (FDA); FDA requests for additional preclinical or clinical data; analyses or changes to study design; or unexpected safety, efficacy, or manufacturing issues;
- clinical trial results may show the product to be less effective than desired or to have harmful or problematic side effects;
- difficulties in formulating the product, scaling the manufacturing process, or getting approval for manufacturing;
- even if safe and effective, manufacturing costs, pricing, reimbursement or competition issues, or other factors may make the product uneconomical;
- proprietary rights of others and their competing products and technologies may prevent the product from being developed or commercialized;
- are not able to compete with superior, equivalent, more cost-effective or more effectively promoted products offered by competitors; or
- competitors may promote their products to a greater extent or more effectively than ours are promoted.

Therefore, our research and development activities, including AzaSite Plus, may not result in any commercially viable products.

***We have a history of operating losses and we expect to continue to have losses in the future***

We have incurred significant operating losses since our inception in 1986 and have pursued numerous drug development candidates that did not prove to have commercial potential. We expect to incur net losses for the foreseeable future or until we are able to achieve significant royalties or other revenues from sales of our products. Attaining significant revenue or profitability depends upon our ability, alone or with third parties, to develop our potential products successfully, conduct clinical trials, obtain required regulatory approvals and manufacture and market our products successfully. We may not ever achieve or be able to maintain significant revenue or profitability, including with respect to AzaSite, our lead product which has not yet been commercially launched outside United States.

***Clinical trials are expensive, time-consuming and difficult to design and implement and it is unclear whether the results of such clinical trials will be favorable***

We have begun our first Phase 3 clinical trial for our AzaSite Plus product candidate. Human clinical trials for our product candidates are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory

requirements. The clinical trial process is also time-consuming. We estimate that clinical trials for AzaSite Plus and any other product candidates may take over a year to complete. Furthermore, we could encounter problems that cause us to abandon or repeat clinical trials resulting in additional expense, further delays and potentially preventing the completion of such trials. The commencement and completion of clinical trials may be delayed or terminated due to several factors, including:

- unforeseen safety issues;

- lack of effectiveness during clinical trials;
- difficulty in determining dosing and trial protocols;
- slower than expected rates of patient recruitment;
- inability to monitor patients adequately during or after treatment; and
- inability or unwillingness of clinical investigators to follow our clinical protocols.

In addition, we or the FDA may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the FDA finds deficiencies in our submissions or the conduct of these trials. In any such case, we may not be able to obtain regulatory approval for our product candidates in which case we would not obtain any benefit from our substantial investment in developing the product and conducting clinical trials for such products.

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

Even if our clinical trials are completed as planned, we cannot be certain that the results will support our product candidate claims. Even if pre-clinical testing and early clinical trials for a product candidate are successful, this does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and pre-clinical testing or meet our expectations. The clinical trial process may fail to demonstrate that our product candidates are safe for humans or effective for indicated uses. In addition, our clinical trials involve relatively small patient populations. Because of the small sample size, the results of these clinical trials may not be indicative of future results. Any such failure would likely cause us to abandon the product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay or preclude the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues.

***Our strategy for commercialization of our products requires us to enter into successful arrangements with corporate collaborators***

We generally intend to enter into future partnering and collaborative arrangements with respect to the commercialization of our product candidates, such as AzaSite Plus. However, we cannot assure you that we will be able to enter into such arrangements or that they will be beneficial to us. The success of our partnering and collaboration arrangements will depend upon many factors, including:

- the progress and results of our preclinical and clinical testing and research and development programs;
- the time and cost involved in obtaining regulatory approvals;
- our ability to negotiate favorable terms with potential collaborators;
- our ability to prosecute, defend and enforce patent claims and other intellectual property rights;
- the outcome of possible future legal actions; and
- competing technological and market developments.

We may not be able to conclude arrangements with third parties to support the commercialization of our products on acceptable terms, or at all, and may not be able to maintain any arrangement that we do enter into.

***The commercial success of our products is dependent on the diligent efforts of our corporate collaborators***

Because we generally rely on third parties for the marketing and sale of our products, revenues that we receive will be highly dependent on the efforts of these third parties, particularly Inspire. These partners may terminate their relationships with us and may not diligently or successfully market or sell our products. These partners may also pursue alternative or competing technologies or develop alternative products either on their own or in collaboration with others, including our competitors. In addition, marketing consultants and contract sales organizations that we may use in the future for our products may market products that compete with our products and we must rely on their efforts and ability to market and sell our products effectively.

***If we fail to enter into future collaborations or our current collaborations are terminated, we will need to enter into new collaborations or establish our own sales and marketing organization***

We may not be able to enter into or maintain collaborative arrangements with third parties. If we are not successful in entering into future collaborations or maintaining our existing collaborations, particularly with Inspire, we may be required to find new corporate collaborators or establish our own sales and marketing organization. Under the terms of the Inspire License, Inspire may terminate the agreement at any time. We have no experience in sales, marketing or distribution and establishing such an organization will be costly. Moreover, there is no guarantee that our sales and marketing organization would be successful once established. If we are unable to enter into additional collaborations or successfully market our products ourselves, our revenues and financial results would be significantly harmed.

***Our future success depends on our ability to engage third parties to assist us with the development of new products, new indications for existing products, and in the conduct of our clinical trials to achieve regulatory approval for commercialization and any failure or delay by those parties to fulfill their obligations could adversely affect our development and commercialization plans***

For our business model to succeed, we must continually develop new products or discover new indications for our existing products. As part of that process, we rely on third parties such as clinical research organizations, clinical investigators and outside testing labs for development activities such as Phase 2 and/or Phase 3 clinical testing and to assist us in obtaining regulatory approvals for our product candidates. We rely heavily on these parties for successful execution of their responsibilities but have no control over how these parties manage their businesses and cannot assure you that such parties will diligently or effectively perform their activities. For example, the clinical investigators conducting our clinical trials, including our current Phase 3 trial for AzaSite Plus, are not our employees. However, we are responsible for ensuring that each of our clinical trials is conducted in accordance with applicable protocols, rules and regulations or in accordance with the general investigational plan and protocols for the trial as well as the various rules and regulations governing clinical trials in the U.S. and abroad. Any failure by those parties to perform their duties effectively and on a timely basis could harm our ability to develop and commercialize new products and harm our business.

***Physicians and patients may not accept and use our products***

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

- perceptions by members of the health care community, including physicians, about the safety and effectiveness of our drugs;
- cost-effectiveness of our products relative to competing products;
- perceived benefits of competing products or treatments;
- physicians' comfort level and prior experience with and use of competing products;
- availability of reimbursement for our products from government or other healthcare payers; and
- effectiveness of marketing and distribution efforts by us and our licensees and distributors.



***We may require additional licenses or be subject to expensive and uncertain patent litigation in order to sell our products***

A number of pharmaceutical and biotechnology companies and research and academic institutions have developed technologies, filed patent applications or received patents on various technologies that may be related to our business. Some of these technologies, applications or patents may conflict with our technologies or patent applications. As is common in the pharmaceutical and biotech industry, from time to time we receive notices from third parties alleging various challenges to our patent rights, and we investigate the merits of each allegation that we receive. Such conflicts, if proven, could invalidate our issued patents, limit the scope of the patents, if any, that we may be able to obtain, result in the denial of our patent applications or block our rights to exploit our technology. If the U.S. Patent and Trademark Office, or USPTO, or foreign patent agencies have issued or in the future issue patents to other companies that cover our activities, we may not be able to obtain licenses to these patents at a reasonable cost, or at all, or be able to develop or obtain alternative technology. If we do not obtain such licenses, we could encounter delays in or be precluded altogether from introducing products to the market. If we are required to obtain additional licenses from third parties with respect to AzaSite Notes in the United States and Canada, we will be required to pay such amounts from our existing cash.

We may need to litigate in order to defend against claims of infringement by others, to enforce patents issued to us or to protect trade secrets or know-how owned or licensed by us. Litigation could result in substantial cost to and diversion of effort by us, which may harm our business, prospects, financial condition, and results of operations. Such costs can be particularly harmful to companies such as ours without significant existing revenue streams or cash resources. We have also agreed to indemnify our licensees against infringement claims by third parties related to our technology, which could result in additional litigation costs and liability for us. In addition, our efforts to protect or defend our proprietary rights may not be successful or, even if successful, may result in substantial cost to us, thereby utilizing our limited resources for purposes other than product development and commercialization.

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

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

***Our business depends upon our proprietary rights, and we may not be able to protect, enforce or secure our intellectual property rights adequately***

Our future success will depend in large part on our ability to obtain patents, protect trade secrets, obtain and maintain rights to technology developed by others, and operate without infringing upon the proprietary rights of others. A substantial number of patents in the field of ophthalmology and genetics have been issued to pharmaceutical, biotechnology and biopharmaceutical companies. Moreover, competitors may have filed patent applications, may have been issued patents or may obtain additional patents and proprietary rights relating to products or processes competitive with ours. Our patent applications may not be approved. We may not be able to develop additional proprietary products that are patentable. Even if we receive patent issuances, those issued patents may not be able to provide us with adequate protection for our inventions or may be challenged by others.

Furthermore, the patents of others may impair our ability to commercialize our products. The patent positions of firms in the pharmaceutical and genetic industries generally are highly uncertain, involve complex legal and factual questions, and have recently been the subject of significant litigation. The USPTO and the courts have not developed, formulated, or presented a consistent policy

regarding the breadth of claims allowed or the degree of protection afforded under pharmaceutical and genetic patents. Despite our efforts to protect our proprietary rights, others may independently develop similar products, duplicate any of our products or design around any of our patents. In addition, third parties from which we have licensed or otherwise obtained technology may attempt to terminate or scale back our rights.

We also depend upon unpatented trade secrets to maintain our competitive position. Others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets. Our trade secrets may also be disclosed, and we may not be able to protect our rights to unpatented trade secrets effectively. To the extent that we, our consultants or our research collaborators use intellectual property owned by others, disputes also may arise as to the rights in related or resulting know-how and inventions.

***In certain circumstances, we may lose the potential to receive future royalty payments after the AzaSite Notes are repaid in full or we may be required to pay damages for breaches of representations, warranties or covenants under certain of the AzaSite Note Financing Agreements.***

In February 2008, through a wholly-owned subsidiary, we issued \$60 million in aggregate principal amount of AzaSite Notes, which are secured principally by royalty payments from future sales of AzaSite in North America, but not the right to receive such payments, and by a pledge by us of all the outstanding equity interest in our subsidiary. If the AzaSite royalty payments are insufficient to repay the AzaSite Notes or if an event of default occurs under the indenture governing the AzaSite Notes, in certain circumstances, the royalty payments and our equity interest in our subsidiary may be foreclosed upon and we would lose the potential to receive future royalty payments after the AzaSite Notes are repaid in full and our intellectual property and other rights related to AzaSite. In addition, in connection with the issuance of the AzaSite Notes, we have made certain representations, warranties and covenants to our subsidiary and the holders of the AzaSite Notes, or the Noteholders. If we breach these representations, warranties or covenants, such breach could trigger an event of default under the indenture and we could also be liable to our subsidiary or the Noteholders for substantial damages in respect of any such breach, which could harm our financial condition and ability to conduct our business as currently planned. See “Business-Recent Events” and Note 12 to the Consolidated Financial Statements included herein for a more complete description of the terms of the AzaSite Notes.

***Inspire’s failure to successfully market and commercialize AzaSite would harm sales of AzaSite and, therefore, would delay or prevent repayment of the AzaSite Notes, which would delay or prevent us from receiving future revenue from sales of AzaSite.***

The AzaSite Notes issued by our subsidiary will be repaid solely from royalties on net sales of AzaSite in the United States and Canada by Inspire under the Inspire Agreement. Inspire has assumed full control of all promotional, sales and marketing activities for AzaSite and has sole control over the pricing of AzaSite. Accordingly, royalty payments in respect of net sales of AzaSite in the United States and, upon regulatory approval, in Canada, will be entirely dependent on the actions, efforts and success of Inspire, over whom neither we nor our subsidiary have control. The success of Inspire’s commercialization of AzaSite and the timely repayment of the AzaSite Notes will depend on a number of factors, including:

- the scope of Inspire’s launch of AzaSite in the United States and Canada;
- the effectiveness and extent of Inspire’s promotional, sales and marketing efforts;
- Inspire’s ability to build, train and retain an effective sales force;
- Inspire’s ability to successfully sell AzaSite to physicians and patients;
- Inspire’s pricing decisions regarding AzaSite;
- Inspire’s marketing and selling of any current or future competing products;
- Inspire’s ability to compete against larger and more experienced competitors;
- the discovery of any side effects or negative efficacy findings for AzaSite;
- product recalls or product liability claims relating to AzaSite;

- the introduction of generic competition;
- if competing products for the treatment of bacterial conjunctivitis obtain more favorable formulary status than AzaSite; and
- the relevant parties' ability to adequately maintain or enforce the intellectual property rights relevant to AzaSite.

Inspire has only recently established its sales force for AzaSite. Inspire has reported that it has incurred substantial expenses in establishing and maintaining its sales force for AzaSite, including substantial additional expenses for the training and management of personnel and the infrastructure to enable its sales force to be effective and compliant with the multiple laws and regulations affecting sales and promotion of pharmaceutical products. Although individual members of the sales force have experience in sales with other companies, Inspire did not have a sales force prior to 2004 and may experience difficulties building and maintaining its sales force, which could harm sales of AzaSite.

Inspire is promoting AzaSite to select eye care professionals, pediatricians and primary care providers. However, Inspire has no prior experience calling on pediatricians and primary care physicians. A large number of pharmaceutical companies, including those with competing products, much larger sales forces and much greater financial resources, and those with products for indications that are completely unrelated to AzaSite, compete for the time and attention of pediatricians and primary care physicians. Neither we nor our subsidiary have any control over how Inspire manages and operates its sales force, how effective Inspire's sales efforts will be or Inspire's pricing decisions regarding AzaSite.

In addition, Inspire depends on three pharmaceutical wholesalers for the vast majority of its AzaSite sales in the United States. These companies are Cardinal Health, McKesson Corporation and AmerisourceBergen. The loss of any of these wholesalers could harm sales of AzaSite. It is also possible that these wholesalers, or others, could decide to change their policies or fees, or both, in the future. This could cause Inspire to incur higher product distribution costs, which would result in lower net sales of AzaSite.

Inspire could experience financial or other difficulties unrelated to AzaSite that could adversely affect the marketing or sale of AzaSite. Moreover, Inspire could change its commercial strategy and deemphasize or sell or sublicense its rights to AzaSite. Neither we nor our subsidiary can prevent Inspire from developing or licensing a product that competes with AzaSite or limiting or withdrawing its support of AzaSite. Our subsidiary's ability to pay amounts due on the AzaSite Notes may be materially harmed to the extent Inspire fails or is unable to successfully market and sell AzaSite. Our ability to receive future revenue from sales of AzaSite is dependent on our subsidiary repaying the AzaSite Notes in a timely fashion. If our subsidiary takes longer than anticipated to repay the AzaSite Notes, or if it defaults on the AzaSite Notes, in each case due to lower sales of AzaSite by Inspire for any of the reasons described above, or due to other unforeseen events, we may not receive future revenue from AzaSite as currently planned, or at all.

***Royalties under the Inspire License Agreement may not be sufficient for our subsidiary to meet its payment obligations under the AzaSite Notes.***

Inspire's obligation to pay royalties on net sales of AzaSite under the Inspire Agreement expires on a country-by-country basis upon the later of 11 years from the first commercial sale of AzaSite, which, in the United States, is August 13, 2018, or when the last valid claim under one of our licensed patents covering a subject product under the Inspire Agreement in the United States and Canada expires. While our subsidiary will be entitled to minimum royalties under the Inspire Agreement from Inspire for five years after the first year of a commercial sale, such minimum royalties will not be sufficient for our subsidiary to meet its payment obligations under the AzaSite Notes and, therefore, it will be dependent on Inspire's successful sales and marketing efforts for AzaSite in order for it to receive royalties in excess of these minimum amounts. In addition, Inspire's obligation to pay minimum royalties is suspended during any period in which (i) the FDA or any other applicable regulatory authority has required any Inspire licensed product to be withdrawn from the market or the marketing thereof otherwise to be suspended in the United States or (ii) Inspire is unable, despite use of commercially reasonable efforts, to obtain supply of any Inspire licensed product in finished form in commercially reasonable amounts necessary to launch or market such Inspire licensed product in the United States.

Royalties under the Inspire Agreement are subject to a cumulative reduction or offset in the event of patent invalidity, generic competition, uncured material breaches by us or in the event that Inspire is required to pay royalties, milestone payments or license fees to third parties for the continued use of AzaSite. The applicable royalty rate is also subject to reduction by up to 50% in any country during any period in which AzaSite does not have patent protection. These cumulative reductions or offsets could result in our

subsidiary receiving significantly reduced or no royalties under the Inspire Agreement, which would delay repayment of the AzaSite Notes, or result in a default under the AzaSite Notes. In such circumstances we may not receive future revenue from AzaSite as currently planned, or at all.

***If the Inspire Agreement is terminated in whole or in part while the AzaSite Notes remain outstanding, we will be forced to find a new third party collaborator for AzaSite, pursue commercialization efforts ourselves or else we will lose our right to certain intellectual property rights related to AzaSite to our subsidiary.***

In February 2008, in connection with our subsidiary's issuance of the AzaSite Notes, we entered into the Residual License Agreement with our subsidiary. Under the terms of the Residual License Agreement, if the Inspire Agreement is terminated in the United States or Canada while the AzaSite Notes are outstanding, all of our rights to AzaSite in such country or countries will be licensed to our subsidiary and we have three months under the terms of the Interim Sublicense, which is a part of the Residual License, to find a new third party collaborator to undertake commercialization efforts with respect to AzaSite or pursue commercialization efforts ourselves in such country or countries. Inspire can terminate the Inspire Agreement unilaterally in a variety of circumstances, including at any time in its discretion. If the Inspire Agreement is terminated, our efforts to find a new third party collaborator or pursue direct commercialization efforts ourselves will divert the attention of senior management from our current business operations, which could delay the development or licensing of our other product candidates. If we elect to commercialize AzaSite ourselves, we may expend significant resources as we currently have no sales, marketing or distribution capabilities or experience, and have no current plans to establish any such resources, which could harm our financial condition and results of operation.

If we are unsuccessful in finding a new third party collaborator for AzaSite or elect not to pursue commercialization efforts ourselves, the Interim Sublicense will terminate and our subsidiary will retain all rights to the intellectual property with respect to AzaSite in the related country or countries in which the Inspire Agreement was terminated. If the Interim Sublicense terminates in accordance with the Residual License Agreement, our subsidiary may grant a sublicense under the license granted under the Residual License Agreement or pursue commercialization efforts itself. In any such circumstances, our subsidiary will remit for payment on the AzaSite Notes any royalties and other payments arising from the exercise of the license under the Residual License Agreement. As all economic value arising from the intellectual property subject to the Inspire Agreement shall remain with our subsidiary (whether or not the Inspire Agreement remains in effect and whether or not our subsidiary continues to be owned by us or our equity in the subsidiary is foreclosed upon by the Noteholders), while the AzaSite Notes are outstanding and following repayment thereof, we may never receive any future royalties or economic benefit from AzaSite and may lose rights to the intellectual property relating thereto.

***We rely on a sole source for the supply of the active pharmaceutical ingredient for AzaSite.***

We currently have a single supplier for azithromycin, the active drug incorporated into AzaSite. Under the Inspire License Agreement and the Inspire Supply Agreement, we have agreed to provide a supply of azithromycin to Inspire for the manufacture of AzaSite in the Territory, which we currently arrange through one supplier. The supplier of azithromycin has a drug master file on the compound with the FDA and is subject to the FDA's review and oversight. The supplier's manufacturing facility is subject to potential natural disasters, including earthquakes, hurricanes, tornadoes, floods, fires or explosions, and other interruptions in operation due to factors including labor unrest or strikes, failures of utility services or microbial or other contamination. If the supplier failed or refused to continue to supply us, if the FDA were to identify issues in the production of azithromycin that the supplier was unable to resolve quickly and cost-effectively, or if other issues were to arise that impact production, Inspire's ability to manufacture and commercialize AzaSite could be interrupted, and our subsidiary's ability to pay amounts due on the AzaSite Notes may be materially harmed, which could prevent or delay our ability to receive future revenue from AzaSite. Additional suppliers for azithromycin exist, but qualification of an alternative source could be time consuming and expensive and, during such qualification process, could negatively impact the sales of AzaSite. There is also no guarantee that these additional suppliers can supply sufficient quantities or quality product at a reasonable price, or at all. While we are required to maintain a certain level of inventory of azithromycin to support Inspire's manufacturing needs, this amount may not be sufficient to prevent an interruption in the availability of AzaSite.

In addition, certain of the raw materials that we use in formulating DuraSite, the drug delivery system used in AzaSite, are available only from Lubrizol Advanced Materials, Inc., or Lubrizol. Although we do not have a current supply agreement with Lubrizol, we have not encountered any difficulties obtaining necessary materials from Lubrizol. Any significant interruption in the supply of these raw materials could delay sales of AzaSite, which could then harm our subsidiary's ability to pay amounts due on the AzaSite Notes and affect our ability to receive future revenue from AzaSite.

***We are dependent upon key employees and we may not be able to retain or attract key employees, and our ability to attract and retain key employees could be harmed by our current financial situation***

We are highly dependent on Dr. S. Kumar Chandrasekaran, who is our chief executive officer and president, and Dr. Lyle Bowman, our vice president, development and operations. The loss of services from either of these key individuals might significantly delay or prevent the achievement of planned development objectives. We carry a \$1.0 million life insurance policy on Dr. Chandrasekaran under which we are the sole beneficiary, however in the event of the death of Dr. Chandrasekaran such policy would be unlikely to fully compensate us for the hardship and expense in finding a successor. We do not carry a life insurance policy on Dr. Bowman. Furthermore, a critical factor to our success will be recruiting and retaining additional qualified personnel. Competition for skilled individuals in the biotechnology business, particularly in the San Francisco Bay Area is highly intense, and we may not be able to continue to attract and retain personnel necessary for the development of our business. Our ability to attract and retain such individuals may be reduced by our current financial situation and our past reductions in force. The loss of key personnel, the failure to recruit additional personnel or to develop needed expertise would harm our business.

***We may not successfully manage growth***

Our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our management and on our administrative, operational and financial resources. To manage this growth, we will have to expand our facilities, augment our operational, financial and management systems and hire and train additional qualified personnel, all of which will cause us to incur significant additional expense and may not be accomplished effectively. If we are unable to manage our growth effectively, our business would be harmed.

***Our products are subject to government regulations and approvals which may delay or prevent the marketing of potential products and impose costly procedures upon our activities***

The FDA and comparable agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon preclinical and clinical testing, manufacturing and marketing of pharmaceutical products. Lengthy and detailed preclinical and clinical testing, validation of manufacturing and quality control processes, and other costly and time-consuming procedures are required. Satisfaction of these requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the pharmaceutical product. The effect of government regulation may be to delay or to prevent marketing of potential products for a considerable period of time and to impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approval on a timely basis, or at all, for any products we develop. Success in preclinical or early stage clinical trials does not assure success in later stage clinical trials. Data obtained from preclinical and clinical activities are susceptible to varying interpretations that could delay, limit or prevent regulatory approval. If regulatory approval of a product is granted, such approval may impose limitations on the indicated uses for which a product may be marketed. Further, even after we have obtained regulatory approval, later discovery of previously unknown problems with a product may result in restrictions on the product, including withdrawal of the product from the market. Moreover, the FDA has recently reduced previous restrictions on the marketing, sale and prescription of products for indications other than those specifically approved by the FDA. Accordingly, even if we receive FDA approval of a product for certain indicated uses, our competitors, including our collaborators, could market products for such indications even if such products have not been specifically approved for such indications. If the FDA determines regulatory approval is required any delay in obtaining or failure to obtain regulatory approvals would make it difficult or impossible to market our products and would harm our business, prospects, financial condition, and results of operations.

The FDA's policies may change and additional government regulations may be promulgated which could prevent or delay regulatory approval of our potential products. Moreover, increased attention to the containment of health care costs in the United States could result in new government regulations that could harm our business. Adverse governmental regulation might arise from future legislative or administrative action, either in the United States or abroad. See "Uncertainties regarding healthcare reform and third-party reimbursement may impair our ability to raise capital, form collaborations and sell our products."

***We have no experience in commercial manufacturing and if contract manufacturing is not available to us or does not satisfy regulatory requirements, we will have to establish our own regulatory compliant manufacturing capability and may not have the financial resources to do so***

We have no experience manufacturing products for Phase 3 and commercial purposes at our own facility. We have a pilot facility licensed by the State of California to manufacture a number of our products for Phase 1 and Phase 2 clinical trials but not for late stage clinical trials or commercial purposes. Any delays or difficulties that we may encounter in establishing and maintaining a relationship with qualified manufacturers to produce, package and distribute our finished products may harm our clinical trials, regulatory filings, market introduction and subsequent sales of our products.

Contract manufacturers must adhere to current Good Manufacturing Practices regulations that are strictly enforced by the FDA on an ongoing basis through the FDA's facilities inspection program. Contract manufacturing facilities must pass a pre-approval plant inspection before the FDA will approve a new drug application. Some of the material manufacturing changes that occur after approval are also subject to FDA review and clearance or approval. While the FDA has approved the AzaSite manufacturing process and facility, the FDA or other regulatory agencies may not approve the process or the facilities by which any of our other products may be manufactured. Our dependence on third parties to manufacture our products may harm our ability to develop and deliver products on a timely and competitive basis. Should we be required to manufacture products ourselves, we:

- will be required to expend significant amounts of capital to install a manufacturing capability;
- will be subject to the regulatory requirements described above;
- will be subject to similar risks regarding delays or difficulties encountered in manufacturing any such products; and
- will require substantially more additional capital than we otherwise may require.

Therefore, we may not be able to manufacture any products successfully or in a cost-effective manner.

***We compete in highly competitive markets and our competitors' financial, technical, marketing, manufacturing and human resources may surpass ours and limit our ability to develop and/or market our products and technologies***

Our success depends upon developing and maintaining a competitive advantage in the development of products and technologies in our areas of focus. We have many competitors in the United States and abroad, including pharmaceutical, biotechnology and other companies with varying resources and degrees of concentration in the ophthalmic market. Our competitors may have existing products or products under development which may be technically superior to ours or which may be less costly or more acceptable to the market. Our competitors may obtain cost advantages, patent protection or other intellectual property rights that would block or limit our ability to develop our potential products. Competition from these companies is intense and is expected to increase as new products enter the market and new technologies become available. Many of our competitors have substantially greater financial, technical, marketing, manufacturing and human resources than we do, particularly in light of our current financial condition. In addition, they may succeed in developing technologies and products that are more effective, safer, less expensive or otherwise more commercially acceptable than any that we have or will develop. Our competitors may also obtain regulatory approval for commercialization of their products more effectively or rapidly than we will. If we decide to manufacture and market our products by ourselves, we will be competing in areas in which we have limited or no experience such as manufacturing efficiency and marketing capabilities.

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

The market for our product candidates is characterized by intense competition and rapid technological advances. If our product candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products fail

to capture and maintain market share, we may not achieve sufficient product revenues and our business will be harmed.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have products competitive with AzaSite already approved or in development, including Zymar and Ocuflax by Allergan, Vigamox and Ciloxan by Alcon, and Quixin by Johnson & Johnson. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking pre-clinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs;
- launching, marketing and selling drugs; and
- attracting qualified personnel, parties for acquisitions, joint ventures or other collaborations.

***Uncertainties regarding healthcare reform and third-party reimbursement may impair our ability to raise capital, form collaborations and sell our products***

The continuing efforts of governmental and third-party payers to contain or reduce the costs of healthcare through various means may harm our business. For example, in some foreign markets the pricing or profitability of health care products is subject to government control. In the United States, there have been, and we expect there will continue to be, a number of federal and state proposals to implement similar government control. The implementation or even the announcement of any of these legislative or regulatory proposals or reforms could harm our business by reducing the prices we or our partners are able to charge for our products impeding our ability to achieve profitability, raise capital or form collaborations. In addition, the availability of reimbursement from third-party payers determines, in large part, the demand for healthcare products in the United States and elsewhere. Examples of such third-party payers are government and private insurance plans. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products, and third-party payers are increasingly challenging the prices charged for medical products and services. If we succeed in bringing one or more products to the market, reimbursement from third-party payers may not be available or may not be sufficient to allow us to sell our products on a competitive or profitable basis.

***Our insurance coverage may not adequately cover our potential product liability exposure***

We are exposed to potential product liability risks inherent in the development, testing, manufacturing, marketing and sale of human therapeutic products. Product liability insurance for the pharmaceutical industry is expensive. Although we believe our current insurance coverage is adequate to cover likely claims we may encounter given our current stage of development and activities, our present product liability insurance coverage will not be adequate to cover all potential claims we may encounter, particularly as AzaSite is commercialized outside the United States and Canada. Once AzaSite is commercialized in other countries, we may have to increase our coverage, which will be expensive and we may not be able to obtain or afford adequate insurance coverage against potential claims in sufficient amounts or at a reasonable cost.

***Our use of hazardous materials may pose environmental risks and liabilities which may cause us to incur significant costs***

Our research, development and manufacturing processes involve the controlled use of small amounts of hazardous solvents used in pharmaceutical development and manufacturing, including acetic acid, acetone, acrylic acid, calcium chloride, chloroform, dimethyl sulfoxide, ethyl alcohol, hydrogen chloride, nitric acid, phosphoric acid and other similar solvents. We retain a licensed outside contractor that specializes in the disposal of hazardous materials used in the biotechnology industry to properly dispose of these materials, but we cannot completely eliminate the risk of accidental contamination or injury from these materials. Our cost for the disposal services rendered by our outside contractor was approximately \$13,400 and \$11,800 for the years ended 2007 and 2006,

respectively. In the event of an accident involving these materials, we could be held liable for any damages that result, and any such liability could exceed our resources. Moreover, as our business develops we may be required to incur significant costs to comply with federal, state and local environmental laws, regulations and policies, especially to the extent that we manufacture our own products.

***If we engage in acquisitions, we will incur a variety of costs, and the anticipated benefits of the acquisitions may never be realized***

We may pursue acquisitions of companies, product lines, technologies or businesses that our management believes are complementary or otherwise beneficial to us. Any of these acquisitions could have a negative effect on our business. Future acquisitions may result in substantial dilution to our stockholders, the expenditure of our current cash resources, the incurrence of additional debt and amortization expenses related to goodwill, research and development and other intangible assets. In addition, acquisitions would involve many risks for us, including:

- assimilating employees, operations, technologies and products from the acquired companies with our existing employees, operations, technologies and products;
- diverting our management's attention from day-to-day operation of our business;
- entering markets in which we have no or limited direct experience; and
- potentially losing key employees from the acquired companies.

If we fail to adequately manage these risks we may not achieve the intended benefits from our acquisitions.

***Management and principal stockholders may be able to exert significant control on matters requiring approval by our stockholders***

As of December 31, 2007, our management and principal stockholders (those owning more than 5% of our outstanding shares) together beneficially owned approximately 33% of shares of common stock. In addition, investors in our March/June 2004 and May 2005 private placements, as a group, owned approximately 13% of our outstanding shares of common stock as of December 31, 2007. If such investors were to exercise the warrants they currently hold, assuming no additional acquisitions, sales or distributions, such investors would own approximately 23% of our outstanding shares of common stock based on their ownership percentages as of December 31, 2007. As a result, these two groups of stockholders, acting together or as individual groups, may be able to exert significant control on matters requiring approval by our stockholders, including the election of all or at least a majority of our Board of Directors, amendments to our charter, and the approval of business combinations and certain financing transactions.

***The market prices for securities of biopharmaceutical and biotechnology companies such as ours have been and are likely to continue to be highly volatile due to reasons that are related and unrelated to our operating performance and progress***

The market prices for securities of biopharmaceutical and biotechnology companies, including ours, have been highly volatile. The market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. In addition, future announcements and circumstances, the status of our relationships or proposed relationships with third-party collaborators, the results of testing and clinical trials, the exercise of outstanding options and warrants that could result in dilution to our current holders of common stock, developments in patent or other proprietary rights of us or our competitors, our or Inspire's failure to meet analyst expectations, any litigation regarding the same, technological innovations or new therapeutic products, governmental regulation, or public concern as to the safety of products developed by us or others and general market conditions, concerning us, our competitors or other biopharmaceutical companies, may have a significant effect on the market price of our common stock. For example, in the fourth quarter of fiscal 2007 our closing stock price fluctuated from a high of \$1.32 to a low of \$0.69. Such fluctuations can lead to securities class action litigation. Securities litigation against us could result in substantial costs and a diversion of our management's attention and resources, which could have an adverse effect on our business.

We have not paid any cash dividends on our common stock, and we do not anticipate paying any dividends on our common stock in the foreseeable future.

***We have adopted and are subject to anti-takeover provisions that could delay or prevent an acquisition of our Company and could prevent or make it more difficult to replace or remove current management***

Provisions of our certificate of incorporation and bylaws may constrain or discourage a third party from acquiring or attempting to acquire control of us. Such provisions could limit the price that investors might be willing to pay in the future for shares of our common stock. In addition, such provisions could also prevent or make it more difficult for our stockholders to replace or remove current management and could adversely affect the price of our common stock if they are viewed as discouraging takeover attempts, business combinations or management changes that stockholders consider in their best interest. Our Board of Directors has the authority to issue up to 5,000,000 shares of preferred stock, or Preferred Stock, 7,070 of which have been designated as Series A Convertible Preferred Stock and 15,000 of which have been designated as Series A-1 Preferred Stock. Our Board of Directors has the authority to determine the price, rights, preferences, privileges and restrictions, including voting rights, of the remaining unissued shares of Preferred Stock without any further vote or action by the stockholders. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of the holders of any Preferred Stock that may be issued in the future. The issuance of Preferred Stock, while providing desirable flexibility in connection with possible financings, acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire a majority of our outstanding voting stock, even if the transaction might be desired by our stockholders. Provisions of Delaware law applicable to us could also delay or make more difficult a merger, tender offer or proxy contest involving us, including Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years unless conditions set forth in the Delaware General Corporation Law are met. The issuance of Preferred Stock or Section 203 of the Delaware General Corporation Law could also be deemed to benefit incumbent management to the extent these provisions deter offers by persons who would wish to make changes in management or exercise control over management. Other provisions of our certificate of incorporation and bylaws may also have the effect of delaying, deterring or preventing a takeover attempt or management changes that our stockholders might consider in their best interest. For example, our bylaws limit the ability of stockholders to remove directors and fill vacancies on our Board of Directors. Our bylaws also impose advance notice requirements for stockholder proposals and nominations of directors and prohibit stockholders from calling special meetings or acting by written consent.

***If earthquakes and other catastrophic events strike, our business may be negatively affected***

Our corporate headquarters, including our research and development and pilot plant operations, are located in the San Francisco Bay area, a region known for seismic activity. A significant natural disaster such as an earthquake would have a material adverse impact on our business, results of operations, and financial condition. If we were able to schedule use of the equipment at our contract manufacturing site we could conduct our pilot plant operations however, we would incur significant additional costs and delays in our product development time-lines.

***We face the risk of a decrease in our cash balances and losses in our investment portfolio***

Our investment policy is structured to limit credit risk and manage interest rate risk. By policy, we only invest in what we view as very high quality debt securities, such as U.S. Government securities. However, the recent uncertainties in the credit markets could prevent us from liquidating our positions in securities that we currently believe constitute high quality investments and could also result in the loss of some or all of our principal if the issuer of such securities defaults on its credit obligations or the necessity of reclassifying current assets. Following completion of our \$60.0 million financing on February 21, 2008, investment income will likely become a more substantial component of our net income. The ability to achieve our investment objectives is affected by many factors, some of which are beyond our control. Our interest income will be affected by changes in interest rates, which are highly sensitive to many factors, including governmental monetary policies and domestic and international economic and political conditions. The outlook for our investment income is dependent on the future direction of interest rates and the amount of cash flows from operations, if any, that are available for investment. Any significant decline in our investment income or the value of our investments as a result of falling interest rates, deterioration in the credit of the securities in which we have invested, or general market conditions, could harm our ability to liquidate our investments, our cash position and our net income.

## Item 1B. Unresolved Staff Comments

None.

## Item 2. Properties

We currently lease approximately 39,123 square feet of research laboratory and office space located in Alameda, California. The facility includes laboratories for formulation, analytical, microbiology, pharmacology, quality control and development as well as a pilot manufacturing plant. The lease expires on December 31, 2013, and may be renewed by us for an additional 5-year term. We believe our existing facilities will be suitable and adequate to meet our needs for the immediate future.

## Item 3. Legal Proceedings

None

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

On October 15, 2007, we held our Annual Meeting of Stockholders at which the stockholders approved:

(1) The election of S. Kumar Chandrasekaran, Ph.D., Mitchell H. Friedlaender, M.D., John L. Mattana, Jon S. Saxe and Anders P. Wiklund to our Board of Directors to serve until the next annual meeting or until their successors are elected and qualified. The following directors received the number of votes set opposite their respective names:

	For Election	Withheld
S. Kumar Chandrasekaran, Ph.D.	57,460,817	9,927,504
Mitchell H. Friedlaender, M.D.	58,396,307	8,992,014
John L. Mattana	57,021,350	10,366,971
Jon S. Saxe	58,183,582	9,204,739
Anders P. Wiklund	57,721,204	9,667,117

(2) Adoption of 2007 Performance Incentive Plan, or the 2007 Plan. Our stockholders voted to approve the proposed adoption of the 2007 Plan. The 2007 Plan provides for grants of stock options and other equity-based awards to employees and consultants that provide services to us and our subsidiaries and to our non-employee directors. No increase was made to the total number of shares of common stock available for issuance under the 2007 Plan. Such proposal received 16,284,261 votes for the 2007 Plan, 8,206,171 votes against the 2007 Plan, 91,547 votes abstaining, and 42,806,342 broker non-votes.

(3) Adoption of the Amended and Restated 1994 Employee Stock Purchase Plan, or the Purchase Plan. The amendments extended the term of the Purchase Plan until August 8, 2017 and made various other changes to conform the Purchase Plan with current market practice. The Purchase Plan provides eligible employees with an opportunity to acquire shares of our common stock on a periodic basis by means of payroll deductions. No increase was made to the total number of shares of common stock available for issuance under the Purchase Plan. Such proposal received 19,050,970 votes for the Purchase Plan, 5,302,532 votes against the Purchase Plan, 228,477 votes abstaining, and 42,806,342 broker non-votes.

(4) The ratification of our audit committee's appointment of Burr, Pilger & Mayer LLP as our independent public accountants for the fiscal year ending December 31, 2007. Such proposal received 65,885,872 votes for ratification, 1,045,632 votes against ratification and 456,817 abstentions.

## Executive Officers of the Company

As of March 14, 2008, our executive officers were as follows:

<u>Name</u>	<u>Age</u>	<u>Title</u>
S. Kumar Chandrasekaran, Ph.D.	65	Chairman of the Board, President, and Chief Executive Officer
Lyle M. Bowman, Ph.D.	59	Vice President, Development and Operations
Louis Drapeau	64	Vice President and Chief Financial Officer
Kamran Hosseini, M.D., Ph.D.	43	Vice President, Clinical Affairs and Chief Medical Officer
David F. Heniges	64	Vice President and General Manager, Commercial Opportunities
Sandra C. Heine	46	Vice President, Finance and Administration

S. Kumar Chandrasekaran joined us in September 1987 as Vice President, Development. From 1988 to 1989, Dr. Chandrasekaran served as Vice President, Research and Development. From 1989 to 1993, he served as President and Chief Operating Officer. Since August 1993, Dr. Chandrasekaran has served as Chairman of the Board of Directors, President and Chief Executive Officer from January 1999 to October 2007, he also served as Chief Financial Officer. Dr. Chandrasekaran holds a Ph.D. in Chemical Engineering from the University of California, Berkeley.

Lyle M. Bowman joined us in October 1988 as Director of Drug Delivery Systems. From 1989 to 1991, Dr. Bowman served as Vice President, Science and Technology. From 1991 to 1995, he served as Vice President, Development, and since 1995 has served as Vice President Development and Operations. Dr. Bowman holds a Ph.D. in Physical Chemistry from the University of Utah.

Louis Drapeau joined us on October 1, 2007 as Vice President and Chief Financial Officer. Mr. Drapeau served as Senior Vice President, Finance and Chief Financial Officer of Nektar Therapeutics, a biopharmaceutical company, from January 2006 until September 2007. From August 2002 to August 2005, Mr. Drapeau was Senior Vice President and Chief Financial Officer of BioMarin Pharmaceutical, a fully integrated biopharmaceutical company. From August 2004 to May 2005, Mr. Drapeau also held the position of Acting Chief Executive Officer of BioMarin. Prior to that, Mr. Drapeau spent over 30 years with Arthur Andersen including 19 years as an Audit Partner in Arthur Andersen's Northern California Audit and Business Consulting practice which also included 12 years as Managing Partner. He holds an undergraduate degree in mechanical engineering and masters in business administration from Stanford University.

Kamran Hosseini joined us on February 11, 2008 as Vice President, Clinical Affairs and Chief Medical Officer. From November 2007 to February 2008, Dr. Hosseini served as the ophthalmic expert at JGB BioPharma consulting for R&D, preclinical, clinical, and business development projects. From May 2005 to October 2007, he was in the ocular drug delivery program at Alza Corporation, a member of the Johnson and Johnson Family of Companies, where he provided ophthalmology and visual science expertise for new technology assessment activities aimed at enhancing the drug/device unit pipeline. From November 2003 to May 2005, he was a post doctoral fellow in retinal degenerative diseases at the University of California, San Francisco. Dr. Hosseini received his M.D. from the University of Groningen Faculty of Medicine, The Netherlands; and his Ph.D. as part of a joint program at the University of Texas, Medical Branch in Galveston and the University of Maastricht, The Netherlands.

David Heniges joined us in July 2002 as Vice President and General Manager, Commercial Opportunities. From 1998 to 2001, Mr. Heniges served as General Manager-Europe/Africa/Middle East for Kera Vision, Inc., a manufacturer of implantable ophthalmic devices and equipment. From 1996 to 1998 he was Vice President, Global Marketing for the cardiovascular group at Baxter Healthcare Corporation. From 1982 to 1995 he served in various managerial positions, including Director, Product Management and International Marketing, Vice President, Marketing, and Vice President, Worldwide Business Development, at IOLAB Corporation, a Johnson & Johnson company, which manufactured ophthalmic devices, equipment and pharmaceuticals. Mr. Heniges spent 23 years in total with Johnson and Johnson in various sales, marketing, and business development positions. Mr. Heniges holds a B.S. in Sociology with a minor in science from Oregon State University.

Sandra C. Heine joined us in March 1997 as Controller. From October 1999 to January 2005, Ms. Heine served as Senior Director of Finance and Administration and since January 2005 has served as Vice President, Finance and Administration. Ms. Heine holds a B.S. in Business Administration from Colorado State University.

Officers are appointed to serve at the discretion of the Board of Directors until their successors are appointed. There are no family relationships between any members of our Board of Directors and our executive officers.

## PART II

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

#### Market Information

Since June 10, 1998, our common stock has traded on The American Stock Exchange under the symbol "ISV." From our initial public offering on October 18, 1993 until June 9, 1998, our common stock traded on The Nasdaq National Market under the symbol "INSV." Prior to our initial public offering, there was no public market for our common stock. The following table sets forth the high and low sales prices for our common stock as reported by The American Stock Exchange for the periods indicated. These prices do not include retail mark-ups, mark-downs or commissions.

<b>2007</b>	<b>High</b>	<b>Low</b>
First Quarter	1.73	1.42
Second Quarter	1.79	1.42
Third Quarter	1.49	1.04
Fourth Quarter	1.32	0.69
<b>2006</b>	<b>High</b>	<b>Low</b>
First Quarter	2.17	0.90
Second Quarter	2.69	1.53
Third Quarter	1.90	1.26
Fourth Quarter	1.88	1.27

#### Dividends

We have never declared or paid dividends on our common stock and do not anticipate paying any cash dividends in the foreseeable future. It is the present policy of our Board of Directors to retain our earnings, if any, for the development of our business.

#### Other Information

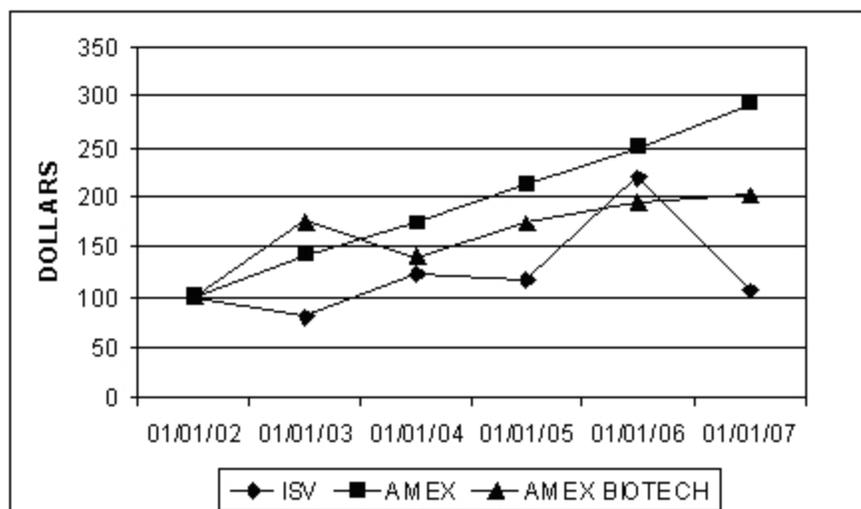
For information regarding securities authorized for issuance under our equity compensation plans, please see Note 9 in the Notes to the Consolidated Financial Statements contained in this Annual Report on Form 10-K.

As of March 12, 2008, we had approximately 210 stockholders of record of our Common Stock. On March 12, 2008, the last sale price reported on The American Stock Exchange for our common stock was \$0.65 per share.

## Stock Performance Graph

The following graph compares the percentage change in (i) the cumulative total stockholder return on our common stock from December 31, 2002 through December 31, 2007 with (ii) the cumulative total return on (a) the American Stock Exchange (U.S. Index) and (b) the American Stock Exchange (biotech) index. The comparison assumes (i) an investment of \$100 on December 31, 2002 in each of the foregoing indices and (ii) reinvestment of dividends, in any.

*The stock price performance shown on the graph below represents historical price performance and is not necessarily indicative of any future stock price performance.*



	ISV	AMEX	AMEX BIOTECH
12/31/02	100	100	100
12/31/03	80	142	175
12/31/04	124	174	140
12/31/05	117	213	175
12/31/06	218	249	194
12/31/07	106	292	202

*Notwithstanding anything to the contrary set forth in any of our previous filings under the Securities Act of 1933 or the Securities Exchange Act of 1934 which might incorporate any of our future filings made under those statutes, the preceding Stock Performance Graph will not be incorporated by reference into any of those prior filings, nor will such graph be incorporated by reference into any of our future filings made under those statutes.*

## Recent Sales of Unregistered Securities

None.

## Issuer Purchases of Securities

None.

**Item 6. Selected Consolidated Financial Data**

The comparability of the following selected financial data is affected by a variety of factors, and this data is qualified by reference to and should be read in conjunction with the audited consolidated financial statements and notes thereto and the Management's Discussion and Analysis of Financial Condition and Results of Operations contained elsewhere in this Annual Report on Form 10-K. The following table sets forth selected consolidated financial data for us for the five years ended December 31, 2007 (in thousands except per share amounts):

(in thousands, except per share data)	<b>Year Ended December 31,</b>				
	<b>2007</b>	<b>2006</b>	<b>2005</b>	<b>2004</b>	<b>2003</b>
<b>Consolidated Statements of Operations Data</b>					
Revenues	\$ 23,761	\$ 2	\$ 4	\$ 542	\$ 134
Cost of revenues	982	28	14	14	20
Operating expenses:					
Research and development	10,384	8,890	10,690	6,788	4,007
General and administrative	6,760	6,182	4,510	3,826	3,450
Total expenses	17,144	15,072	15,200	10,614	7,457
Gain on sale of assets	-	-	-	4,616	1,153
Interest (expense) and other income, net	(100)	(1,513)	(5)	(44)	(561)
Net income (loss)	5,535	(16,611)	(15,215)	(5,514)	(6,751)
Non cash preferred dividend	-	-	-	-	221
Net income (loss) applicable to common stockholders	\$ 5,535	\$ (16,611)	\$ (15,215)	\$ (5,514)	\$ (6,972)
Net income (loss) per share:					
Earnings (loss) per share - basic	\$ 0.06	\$ (0.19)	\$ (0.21)	\$ (0.11)	\$ (0.27)
Earnings (loss) per share - diluted	\$ 0.06	\$ (0.19)	\$ (0.21)	\$ (0.11)	\$ (0.27)
Weighted average shares used in per-share calculation:					
- basic	94,168	88,339	72,647	47,984	25,767
- diluted	100,110	88,339	72,647	47,984	25,767

(in thousands)	<b>As of December 31,</b>				
	<b>2007</b>	<b>2006</b>	<b>2005</b>	<b>2004</b>	<b>2003</b>
<b>Consolidated Balance Sheet Data:</b>					
Cash and cash equivalents	\$ 11,532	\$ 986	\$ 4,027	\$ 5,351	\$ 1,045
Working capital, exclusive of deferred revenue	9,589	(6,836)	(3,424)	3,515	(6,434)
Total assets	15,012	2,439	5,079	5,696	1,405
Long-term Notes Payable	-	-	-	-	16
Accumulated deficit	(147,527)	(153,062)	(136,451)	(121,236)	(115,722)
Total stockholders' equity (deficit)	\$ 746	\$ (6,302)	\$ (2,545)	\$ 3,601	\$ (6,200)

No cash dividends have been declared or paid by us since our inception.

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

The following discussion should be read in conjunction with the financial statements and notes thereto included in Item 8 of this Form 10-K.

### Overview

Historically we have been an ophthalmic product development company focused on ophthalmic pharmaceutical products based on our proprietary DuraSite® drug delivery technology. Beginning in 2007, we have expanded beyond ophthalmic products to other topical anti-infectives, including the treatment of ear infections. Our intent is to continue to solidify our franchise in ocular anti-infective topical therapies as well as extend our anti-infective platform to non-ocular topical products.

Our DuraSite® sustained delivery technology is a proven, patented synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a solution, gel or suspension and can be customized for delivering a wide variety of potential drug candidates. We are currently focusing our research and development and commercial efforts on the following topical anti-infective products that formulate the antibiotic azithromycin with our DuraSite® drug delivery technology.

- AzaSite® (azithromycin ophthalmic solution) 1% (ISV-401), a DuraSite formulation of azithromycin, was developed to serve as a broad spectrum ocular antibiotic; approved by the FDA in April 2007 to treat bacterial conjunctivitis (pink eye); and launched by Inspire Pharmaceuticals in August 2007. The key advantages are a significantly reduced dosing regimen leading to better compliance and outcome, with a broad spectrum antibiotic, and a lowered probability of bacterial resistance based on high tissue concentration.
- AzaSite Plus™ (ISV-502), a DuraSite formulation of azithromycin and a corticosteroid is under development for ocular inflammation and infection, or blepharoconjunctivitis, for which there is no FDA approved indicated treatment; we initiated a pivotal Phase 3 trial in December 2007.
- AzaSite Otic™ (ISV-016), a DuraSite formulation of azithromycin and a corticosteroid, is under development for the treatment of bacterial infections of the middle ear (otitis media); and is in preclinical development.
- AzaSite Xtra™ (ISV-405), a DuraSite formulation with a higher percentage of azithromycin, is in preclinical development for the treatment of ocular infection and is targeted at international markets.

### Major Developments in 2007

In 2007 our primary developments were related to our AzaSite product and included:

- receipt of \$13.0 million from Inspire upon the February 15, 2007 licensing to Inspire of the manufacturing, sales and marketing and future development rights to AzaSite for the United States and Canada;
- NDA approval of AzaSite by the FDA on April 27, 2007, which triggered a \$19.0 million milestone payment from Inspire;
- launch of AzaSite in the United States by Inspire in August 2007 and recognition of our first royalties in the third quarter of 2007; and
- entrance into our first international licensing agreement for AzaSite with Shin Poong in December 2007.

In 2007 we also continued our development of several additional product candidates that incorporate our DuraSite sustained delivery technology and azithromycin, including:

- successful completion of a Phase 1 clinical trial for our AzaSite Plus product candidate;
- initiation of an AzaSite Plus pivotal Phase 3 trial in December 2007; and

- preclinical development activities for the AzaSite Otic product candidate.

## **Business Strategy**

Our business strategy is to in-license promising product candidates and technologies from academic institutions and other companies and apply our formulation expertise to create novel differentiated product opportunities, subsequently conduct preclinical and clinical testing, and partner with pharmaceutical companies in the late stages of clinical trials to manufacture, market and sell our products. For select opportunities, we may manufacture, market and sell our own products.

We also have internally developed DuraSite-based product candidates using either non-proprietary drugs or compounds developed by others for non-ophthalmic indications. Currently we are leveraging our success with the DuraSite-azithromycin product platform to develop additional ocular and non-ocular topical anti-infective products. As with in-licensed product candidates, we either have partnered or generally plan to partner with pharmaceutical companies to complete clinical development and commercialization of our product candidates.

## **Critical Accounting Policies and Use of Estimates**

The preparation of financial statements in conformity with generally accepted accounting principles in the United States requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

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 significant estimates, assumptions and judgments about matters that are uncertain:

Revenue Recognition. We recognize revenue in accordance with Securities and Exchange Commission Staff Accounting Bulletin No. 104, Revenue Recognition, or SAB 104. SAB 104 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectibility is reasonably assured. Arrangements with multiple elements are accounted for in accordance with Emerging Issues Task Force, or EITF, Issue No. 00-21, Revenue Arrangements with Multiple Deliverables. We analyze our multiple element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting in accordance with EITF 00-21. Our revenues are primarily related to our licensing agreements, and such agreements may provide for various types of payments to us, including upfront payments, research funding and related fees during the term of the agreement, milestone payments based on the achievement of established development objectives, licensing fees, and royalties on product sales.

Upfront, non-refundable payments under licensing agreements are recorded as deferred revenues once received and recognized ratably over the period related activities are performed. Revenues from non-refundable milestones are recognized when the earnings process is complete and the payment is reasonably assured. Non-refundable milestone payments related to arrangements under which we have continuing performance obligations are recognized ratably over the period related activities are performed.

Revenue related to contract research services is recognized when the services are provided and collectibility is reasonable assured.

We receive royalties from licensees based on third-party sales and the royalties are recorded as earned in accordance with the contract terms when third-party results are reliably measured and collectibility is reasonably assured.

Revenues related to sales of the OcuGene glaucoma genetic test, were recognized when all related services had been rendered and collectibility was reasonably assured. Accordingly, revenues for sales of OcuGene may have been recognized in a later period than the associated recognition of costs of the services provided, especially during the initial launch of the product.

Inventory. Our inventories are stated at the lower of cost or market. The cost of the inventory is based on the first-in first-out method. If the cost of the inventory exceeds the expected market value, a provision is recorded for the difference between cost and market.

Income Taxes. Effective January 1, 2007, we adopted the provisions of Financial Accounting Standard Board, Financial Interpretation No. 48, *Accounting for Uncertainty in Income Taxes — an interpretation of FASB Statement No. 109*, or FIN 48. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS No. 109, *Accounting for Income Taxes*, or SFAS 109. The interpretation applies to all tax positions accounted for in accordance with SFAS 109 and requires a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken, or expected to be taken, in an income tax return. Subsequent recognition, derecognition and measurement is based on management's best judgment given the facts, circumstances and information available at the reporting date.

We file U.S. federal and California state income tax returns. To date, we have not been audited by the Internal Revenue Service or any state.

Our policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense. To date, there have been no interest or penalties charged to us in relation to the underpayment of income taxes.

We have generated net losses through the year ended December 31, 2006 and, accordingly, did not record a provision for income taxes. For the year ended December 31, 2007, we generated net income and were able to offset it with our accumulated net operating losses, or NOLs. As of December 31, 2007, our total deferred tax assets were \$54.3 million. The deferred tax assets were primarily comprised of federal and state tax NOL carryforwards. Due to uncertainties surrounding our ability to continue to generate future taxable income to realize these tax assets, a full valuation allowance has been established to offset our deferred tax assets. Additionally, the future utilization of our NOL carryforwards to offset future taxable income is subject to an annual limitation as a result of ownership changes that have occurred previously and may be further impacted by future ownership changes. As necessary, the deferred tax assets have been reduced by any carryforwards that expire prior to utilization as a result of such limitations, with a corresponding reduction of the valuation allowance. These carryforwards may be further reduced if we have any additional ownership changes in the future.

Stock-Based Compensation. In 2007 we granted stock-based awards to eligible employees and directors to purchase shares of our common stock under our stock compensation plan approved in 1994 (the 1994 Plan) and its successor the 2007 Performance Incentive Plan (the 2007 Plan) approved in October 2007. In addition, we have a qualified employee stock purchase plan in which eligible employees may elect to withhold up to 15% of their compensation to purchase shares of our common stock on a quarterly basis at a discounted price equal to 85% of the lower of the employee's offering price or the closing price of the stock on the date of purchase. The benefits provided by these plans qualify as stock-based compensation under the provisions of Statement of Financial Accounting Standards No. 123 (revised 2004), "Share-Based Payment" (SFAS 123R), which requires us to recognize compensation expense based on their estimated fair values determined on the date of grant for all stock-based awards granted, modified or cancelled as of January 1, 2006 (the effective date). Prior to the effective date, we did not recognize any compensation cost in our income statements for stock-based awards granted with an option price equal to the fair market value of our common stock on the date of grant or employee stock purchase rights as we accounted for them under the recognition and measurement principles of APB Opinion No. 25, "Accounting for Stock Issued to Employees" (APB 25) and its related interpretations and adopted the disclosure only provisions of Statement of Financial Accounting Standards No. 123, "Stock-Based Compensation" (SFAS 123).

For the year ended December 31, 2007, we recognized \$1.0 million of compensation expense for employee stock options and purchase rights. At December 31, 2007, we had \$1.8 million in unrecognized compensation cost related to employee stock options remaining, which is expected to be recognized over a weighted average period of 2.3 years.

We estimate the fair value of share-based awards on the date of grant using the Black-Scholes option-pricing method (Black-Scholes method), which was also used for the proforma information required to be disclosed under SFAS 123. The determination of fair value of share-based awards using an option-pricing model requires the use of certain estimates and assumptions that affect the reported amount of share-based compensation cost recognized in our Consolidated Statements of Income. These include estimates of the expected term of share-based awards, expected volatility of our stock price, expected dividends and the risk-free interest rate. These estimates and assumptions are highly subjective and may result in materially different amounts should circumstances change and we employ different assumptions in our application of SFAS 123R in future periods.

For stock-based awards issued during the year ended December 31, 2007, we estimated the expected term by considering various factors including the vesting period of options granted and employees' historical exercise and post-employment termination behavior. Expected volatility is based on the combination of historical volatility of the Company's common stock and the common stock of the Company's competitors, the expected moderation in future volatility over the period commensurate with the expected life of the options and other factors. We have never declared or paid any cash dividends on our common stock and currently do not anticipate paying such cash dividends. We currently anticipate that we will retain all of our future earnings for use in the development and expansion of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our Board of Directors and will depend upon our results of operations, financial condition, financial covenants, tax laws and other factors as the Board of Directors, in its discretion, deems relevant. The risk-free interest rate is based upon U.S. Treasury securities with remaining terms similar to the expected term of the stock-based awards.

## Results of Operations

### *Revenues.*

We had total revenues of \$23.8 million, \$2,000, and \$4,000 for the years ended December 31, 2007, 2006 and 2005, respectively. \$22.1 million of our revenues in 2007 represented the amortization of the license fee and milestone payments for AzaSite that we received from Inspire in February and April 2007, respectively. \$701,000 of our revenues represented royalties from 2007 net sales of AzaSite by Inspire through December 31, 2007. The remainder of our 2007 revenues represented sales of materials to Inspire under the Supply Agreement, sales of our AzaSite finished goods inventory to Inspire and contract services provided to Inspire related to their AzaSite activities. Revenues for 2006 and 2005 were from sales of OcuGene.

### *Cost of revenues.*

Our cost of revenues was \$1.0 million, \$28,000 and \$14,000 for 2007, 2006 and 2005, respectively. Cost of revenues for 2007 reflects royalties accrued for third parties, including Pfizer, through December 31, 2007, the cost of the azithromycin supplied to Inspire under the Supply Agreement and the cost of the AzaSite inventory sold to Inspire. Cost of revenues in 2006 and 2005 reflected the cost of OcuGene tests performed as well as the cost of sample collection kits distributed for use.

### *Research and development (R & D).*

Our R&D activities can be separated into two major segments, research and clinical development. Research includes activities involved in evaluating a potential product, related preclinical testing and manufacturing. Clinical development includes activities related to filings with the FDA and the related human clinical testing required to obtain marketing approval for a potential product. We estimate that the following represents the approximate cost of these activities for 2007, 2006 and 2005 (in thousands):

	<b>As of December 31,</b>		
	<b>2007</b>	<b>2006</b>	<b>2005</b>
Research	\$ 4,372	\$ 3,291	\$ 2,142
Clinical development	6,012	5,599	8,548
<b>Total research and development</b>	<b>\$ 10,384</b>	<b>\$ 8,890</b>	<b>\$ 10,690</b>

Research and development expenses increased to \$10.4 million in 2007 from \$8.9 million in 2006. In 2007 our activities primarily included production of AzaSite process validation batches, expenses related to the AzaSite Canadian NDS filing, AzaSite Plus preclinical activities, Phase 1 clinical trial data evaluation, pilot study, Phase 3 clinical trial design and initiation and preclinical work on AzaSite Otic and AzaSite Xtra. Our R&D personnel costs were higher in 2007 due to success bonuses related to the successful FDA approval of AzaSite. In 2006, our activities had been primarily related to the AzaSite clinical trials, preparation of the related NDA and the FDA filing fee.

Research and development expenses decreased to \$8.9 million in 2006 from \$10.7 in 2005. Costs related to clinical research organizations and the microbiological testing related to our AzaSite Phase 3 clinical trials decreased approximately 71% due to the completion of the trials in January 2006. Costs related to additional headcount, consultants and temporary labor to assist with the preparation of the AzaSite NDA and to file the AzaSite Plus IND offset these expense decreases. Preclinical costs related to the AzaSite Plus program, the manufacture of the AzaSite Plus Phase 1 clinical trial supplies and preparation to manufacture AzaSite Phase 3 clinical units at our contract manufacturing site also partially offset this decrease in external clinical costs in 2006. Additionally, in 2006 we incurred approximately \$245,000 of non-cash expense related to the adoption of FAS 123R and the expensing of options granted to employees and our employee stock purchase plan.

Our future research and development expenses will depend on the results and magnitude or cope of our clinical, preclinical and research activities and requirements imposed by regulatory agencies. Accordingly, our research and development expense 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.

#### *General and administrative.*

General and administrative expenses increased to \$6.8 million in 2007 from \$6.2 million in 2006. This increase mainly reflects higher personnel related expenses associated with an increase in headcount, payment of bonuses upon the approval of the AzaSite NDA, salary and health insurance cost increases and higher non-cash stock-based compensation in the second year after implementation of FAS123R. These increases were partially offset by the decrease in the deferred debt issuance costs related to the short-term Senior Secured Notes which were repaid in February 2007.

General and administrative expenses increased to \$6.2 million in 2006 from \$4.5 million in 2005. This increase mainly reflects the amortization of deferred debt issuance costs related to our short-term Senior Secured Notes, consulting costs related to compliance with Section 404 of the Sarbanes-Oxley Act of 2002 and approximately \$565,000 of non-cash expense related to the adoption of FAS 123R and the related expensing of options granted to directors and employees and our employee stock purchase plan.

#### *Interest, other income (expenses), net.*

Interest expense and other income was an expense of \$100,000, \$1.5 million and \$5,000 in 2007, 2006 and 2005, respectively. In February 2007, our Senior Secured Notes were repaid in full and, correspondingly, interest expense decreased compared to 2006 when these notes were outstanding for the full period. The increased expense in 2006 mainly reflects accrued interest payable on our short-term Senior Secured Notes issued in December 2005 and January 2006 and the accretion of the value of the debt discount related to the warrants issued as part of the note financing.

Interest paid in the future will increase and the amount will be dependent on the repayment of the notes issued in February 2008 secured by royalties received from Inspire for the sales of AzaSite. Interest earned will be dependent on prevailing interest rates and the amount of funds we use for our operating activities.

### **Liquidity and Capital Resources**

We have financed our operations since inception primarily through private placements and public offerings of debt and equity securities, debt financings, equipment and leasehold improvement financing and payments from corporate collaborations. At December 31, 2007, our unrestricted cash and cash equivalents were \$11.5 million. It is our policy to invest our cash and cash equivalents in highly liquid securities, such as interest-bearing money market funds, Treasury and federal agency notes. The current uncertain credit markets may affect the liquidity of such money market funds or other cash investments.

For the year ended December 31, 2007, cash provided by operating activities was \$17.6 million, primarily due to \$32.0 million of license and milestone payments from the February 2007 license of AzaSite to Inspire. For the years ended December 31, 2006 and 2005, cash used for operating activities was \$16.2 million and \$13.4 million, respectively.

Cash used in investing activities was \$1.0 million, \$322,000 and \$137,000, for 2007, 2006 and 2005, respectively, primarily related to cash outlays for additions to laboratory and other equipment.

Cash used in financing activities was \$6.1 million for the year ended December 31, 2007, primarily due to the repayment of short-term notes payable in February 2007. Cash provided by financing activities was \$13.5 million and \$12.2 million for the years ending December 31, 2006 and 2005, respectively, principally due to warrant and option exercises, private placement equity offerings and debt issuances.

The tables below set forth the amount of cash that we raised for fiscal years 2005 through 2007 from warrant and option exercises, stock purchases under our employee stock purchase plan, equity financings and debt financings.

*Cash received from Warrant and Option Exercises and Employee Stock Purchase Plans*

<b>Year</b>	<b>Net Proceeds</b>
2007	\$ 512,000
2006	\$ 5.8 million
2005	\$ 536,000

*Cash Received from Private Placements of Equity Securities*

<b>Date</b>	<b>Net Proceeds</b>	<b>Shares of Common Stock Issued</b>
August 2006	\$5.8 million	4.8 million plus warrants to purchase 1.0 million shares
May 2005	\$8.1 million	16.4 million plus warrants to purchase 4.9 million shares

*Cash Received from Private Placement of Notes*

<b>Date</b>	<b>Net Proceeds</b>	<b>Type of Notes</b>	<b>Interest Rates and Terms</b>	<b>Maturity Date</b>
January 2006	\$1.8 million	Short-Term Senior Secured Notes	10% through July 10, 2006, 12% from July 11, 2006 through February 15, 2007	February 15, 2007*
December 2005	\$3.8 million	Short-Term Senior Secured Notes	10% through June 30, 2006, 12% from July 1, 2006 through February 15, 2007	February 15, 2007*

\* On February 15, 2007, we repaid and redeemed all outstanding principal and interest due under such Notes.

In addition to the above, in 2005 we repaid \$73,000 of short-term notes payable to directors, members of senior management and other stockholders, with interest at rates from 2% to 12% and which matured on March 31, 2007. We received payments on a note from a stockholder of \$168,000 and \$19,000 in 2006 and 2005, respectively.

Our future capital expenditures and requirements will depend on numerous factors, including the progress of our clinical testing, research and development programs and preclinical testing, the time and costs involved in obtaining regulatory approvals, our ability to successfully commercialize AzaSite, AzaSite Plus, OcuGene and any other products that we may launch in the future, our ability to establish collaborative arrangements, the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights, competing technological and market developments, changes in our existing collaborative and licensing relationships, acquisition of new businesses, products and technologies, the completion of commercialization activities and arrangements, and the purchase of additional property and equipment.

We anticipate no material capital expenditures to be incurred for environmental compliance in fiscal year 2008. Based on our environmental compliance record to date, and our belief that we are current in compliance with applicable environmental laws and regulations, environmental compliance is not expected to have a material adverse effect on our operations.

See - Subsequent Event for discussion of our February 21, 2008, issuance of \$60.0 million of notes.



## Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements that have or are reasonably likely to have a current or future material effect.

## Contractual Obligations

The following table summarizes our significant contractual obligations as of December 31, 2007 and the effect such obligations are expected to have on our liquidity and cash flows in future periods. Some of these amounts are based on management's estimates and assumptions about these obligations including their duration, the possibility of renewal and other factors. Because these estimates are necessarily subjective, our actual payments in the future may vary from those listed in this table.

	Payments due by period (in thousands)				
	Total	Less than 1 year	1-3 years	3-5 Years	More than 5 years
Capital Lease Obligations (1)	\$ 58	\$ 18	\$ 35	\$ 5	\$ -
Facilities Lease Obligations (2)	4,728	731	1,529	1,620	848
Purchase obligations (3)	11,007	8,460	2,547	-	-
Licensing agreement obligations (4)	9,475	20	2,175	4,520	2,760
Total commitments	\$ 25,268	\$ 9,229	\$ 6,286	\$ 6,145	\$ 3,608

- (1) We lease our telephones and telephone equipment under two capital lease agreements which expire in 2011.
- (2) We lease our facilities under a non-cancelable operating lease that expires in 2013.
- (3) Purchase obligations include commitments related to clinical development, consulting contracts, manufacturing activities, equipment maintenance, and other significant purchase commitments.
- (4) We have entered into certain license agreements that require us to make minimum royalty payments for the life of the licensed patents. The life of the patents which may be issued and covered by the license agreements cannot be determined at this time, but the minimum royalties due under certain of these agreements are as noted for 2008 through 2017.

## Subsequent Event

In February 2008, our wholly-owned subsidiary issued \$60.0 million in aggregate principal amount of non-convertible, non-recourse promissory notes due in 2019. The notes are secured by, and will be repaid from, royalties to be paid to us by Inspire Pharmaceuticals from sales of AzaSite in the United States and Canada. The annual cash coupon rate on the notes is 16% with interest payable quarterly in arrears beginning May 15, 2008. Net proceeds to InSite from the financing were slightly over \$50.0 million after deducting transaction costs and setting aside \$5.0 million as interest reserves. This interest reserve will be reflected as restricted cash on our balance sheets commencing March 31, 2008.

When the AzaSite royalties received for any quarter exceed the interest payments and certain expenses due that quarter, the excess will be applied to the repayment of principal of the notes until the notes have been paid in full. The notes may be redeemed at our option, subject to the payment of a redemption premium through May 2012. After that date they may be redeemed without a premium.

## Recent Accounting Pronouncements

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 157, or SFAS No. 157, "Fair Value Measurements." SFAS No. 157 provides guidance for using fair value to measure assets and liabilities. It also responds to investors' request for expanded information about the extent to which companies measure assets and liabilities at fair value, the information used to measure fair value, and the effect of fair valued measurements on earnings. SFAS No. 157 applies whenever standards require (or permit) assets or liabilities to be measured at fair value, and does not expand the use of fair value in any new circumstances. SFAS No. 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007, and interim periods

within those fiscal years, with early adoption permitted, except for the impact of FASB Staff Position (FSP) 157-2. FSP 157-2 deferred the adoption of SFAS 157 for non financial assets and liabilities until years ended after November 15, 2008. The Company must adopt these requirements no later than the first quarter of 2008. We do not anticipate the adoption of SFAS No. 157 will have a material effect on our consolidated financial position, results of operations or liquidity.

In February 2007, the FASB issued SFAS No. 159, “The Fair Value Option for Financial Assets and Financial Liabilities — Including an amendment of FASB Statement No. 115,” or SFAS No. 159. SFAS No. 159 expands the use of fair value accounting but does not affect existing standards that require assets or liabilities to be carried at fair value. Under SFAS No. 159, a company may elect to use fair value to measure accounts and loans receivable, available-for-sale and held-to-maturity securities, equity method investments, accounts payable, guarantees and issued debt. Other eligible items include firm commitments for financial instruments that otherwise would not be recognized at inception and non-cash warranty obligations where a warrantor is permitted to pay a third party to provide the warranty goods or services. If the use of fair value is elected, any upfront costs and fees related to the item must be recognized in earnings and cannot be deferred (e.g., debt issue costs). The fair value election is irrevocable and generally made on an instrument-by-instrument basis, even if a company has similar instruments that it elects not to measure based on fair value. At the adoption date, unrealized gains and losses on existing items for which fair value has been elected are reported as a cumulative adjustment to beginning retained earnings. Subsequent to the adoption of SFAS No. 159, changes in fair value are recognized in earnings. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. We are currently determining whether fair value accounting is appropriate for any of our eligible items and cannot estimate the impact, if any, that SFAS No. 159 will have on our consolidated financial position, results of operations or liquidity.

In November 2007, the FASB ratified Issue No. EITF 07-1, “Accounting for Collaborative Agreements Related to the Development and Commercialization of Intellectual Property,” or EITF Issue No. 07-1. EITF Issue No. 07-1 defines collaborative agreements as a contractual arrangement in which the parties are active participants to the arrangement and are exposed to the significant risks and rewards that are dependent on the ultimate commercial success of the endeavor. Additionally, it requires that revenue generated and costs incurred on sales to third parties as it relates to a collaborative agreement be recognized as gross or net based on EITF Issue No. 99-19, “Reporting Revenue Gross as a Principal versus Net as an Agent.” It also requires payments between participants to be accounted for in accordance with already existing generally accepted accounting principles, unless none exist, in which case a reasonable, rational, consistent method should be used. EITF Issue No. 07-1 is effective for fiscal years beginning after December 15, 2008 for all collaborative arrangements existing as of that date, with retrospective application to all periods. We do not anticipate the adoption of EITF Issue No. 07-1 will have a material effect on our financial position, results of operations or liquidity.

In June 2007, the FASB ratified Emerging Issues Task Force Issue No. 07-3, “Accounting for Non-Refundable Payments for Goods or Services Received for Use in Future Research and Development Activities,” or EITF Issue No. 07-3. EITF Issue No. 07-3 requires that nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities be deferred and capitalized and recognized as an expense as the goods are delivered or the related services are performed. EITF Issue No. 07-3 is effective, on a prospective basis, for fiscal years beginning after December 15, 2007. We do not anticipate the adoption of EITF Issue No. 07-3 will have a material effect on our consolidated financial position, results of operations or liquidity.

In December 2007, the FASB issued SFAS No. 141(R), “Business Combinations,” or SFAS No. 141(R). SFAS No. 141(R) changes the requirements for an acquirer’s recognition and measurement of the assets acquired and liabilities assumed in a business combination, including the treatment of contingent consideration, pre-acquisition contingencies, transaction costs, in-process research and development and restructuring costs. In addition, under SFAS No. 141(R), changes in an acquired entity’s deferred tax assets and uncertain tax positions after the measurement period will impact income tax expense. This statement is effective with respect to business combination transactions for which the acquisition date is after December 31, 2008.

In December 2007, the FASB issued SFAS No. 160, “Noncontrolling Interests in Consolidated Financial Statements (an amendment of Accounting Research Bulletin, or ARB, No. 51),” or SFAS No. 160. SFAS No. 160 requires that noncontrolling (minority) interests be reported as a component of equity, that net income attributable to the parent and to the non-controlling interest be separately identified in the income statement, that changes in a parent’s ownership interest while the parent retains its controlling interest be accounted for as equity transactions, and that any retained noncontrolling equity investment upon the deconsolidation of a subsidiary be initially measured at fair value. This statement is effective for fiscal years beginning after December 31, 2008, and shall be applied prospectively. However, the presentation and disclosure requirements of SFAS No. 160 are required to be applied retrospectively for all periods presented. The retrospective presentation and disclosure requirements of this statement will be applied to any prior periods presented in financial statements for the fiscal year ending December 31, 2009, and later periods during which we have a consolidated subsidiary with a noncontrolling interest. As of December 31, 2007, we do not have any consolidated subsidiaries in which there is a noncontrolling interest.



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

The following discusses our exposure to market risk related to changes in interest rates.

We invest our excess cash in investment grade, interest-bearing securities. At December 31, 2007, we had \$11.5 million invested in interest bearing operating accounts. While a hypothetical decrease in market interest rates by 10 percent from the December 31, 2007 levels would cause a decrease in interest income, it would not result in a loss of the principal. Additionally, the decrease in interest income would not be material. The current uncertain credit markets may affect the liquidity of such money market funds or other cash investments.

## Item 8. Financial Statements and Supplementary Data

The following Consolidated Financial Statements and Report of Independent Registered Public Accounting Firm are included on the pages that follow:

	<u>Page</u>
Report of Independent Registered Public Accounting Firm	40
Consolidated Balance Sheets - December 31, 2007 and 2006	41
Consolidated Statements of Operations for the Years Ended December 31, 2007, 2006 and 2005	42
Consolidated Statements of Stockholders' Equity (Deficit) for the Years ended December 31, 2007, 2006 and 2005	43
Consolidated Statements of Cash Flows for the Years Ended December 31, 2007, 2006 and 2005	44
Notes to the Consolidated Financial Statements	45 - 60

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of  
InSite Vision Incorporated

We have audited the accompanying consolidated balance sheets of InSite Vision Incorporated and its subsidiaries (the “Company”) as of December 31, 2007 and 2006, and the related consolidated statements of operations, stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2007. These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of InSite Vision Corporation as of December 31, 2007 and 2006, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2007, in conformity with accounting principles generally accepted in the United States of America.

As discussed in Note 1 and Note 9 to the consolidated financial statements, on January 1, 2006 the Company changed its method of accounting for stock-based compensation as a result of adopting Statement of Financial Accounting Standards No. 123 (revised 2004), “Share-Based Payment” applying the modified prospective method.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of the Company’s internal control over financial reporting as of December 31, 2007, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 17, 2008 expressed an unqualified opinion thereon.

/s/ Burr, Pilger & Mayer LLP  
Palo Alto, California  
March 17, 2008

**INSITE VISION INCORPORATED**  
**CONSOLIDATED BALANCE SHEETS**

(in thousands, except share and per share amounts)	December 31,	
	2007	2006
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 11,532	\$ 986
Restricted cash and cash equivalents	75	75
Accounts receivable	719	-
Deferred debt issuance cost	-	22
Prepaid deal expenses	538	-
Prepaid expenses and other current assets	810	795
<b>Total current assets</b>	<b>13,674</b>	<b>1,878</b>
Property and equipment, at cost:		
Laboratory and other equipment	1,210	580
Leasehold improvements	289	5
Furniture and fixtures	160	77
	1,659	662
Accumulated depreciation	321	101
	1,338	561
<b>Total assets</b>	<b>\$ 15,012</b>	<b>\$ 2,439</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)</b>		
Current liabilities:		
Short-term notes payable to related parties, unsecured	\$ -	\$ 35
Short-term notes payable to related parties, secured	-	231
Short-term notes payable, secured	-	6,300
Accrued interest	-	702
Accounts payable	2,196	377
Accrued liabilities	862	381
Accrued compensation and related expense	979	648
Deferred revenue	10,145	-
Other current liabilities	48	18
<b>Total current liabilities</b>	<b>14,230</b>	<b>8,692</b>
Capital lease obligation, less current portion	36	49
<b>Total liabilities</b>	<b>14,266</b>	<b>8,741</b>
Commitments and contingencies (Note 6)		
Stockholders' equity (deficit):		
Preferred stock, \$0.01 par value, 5,000,000 shares authorized, none issued and outstanding at December 31, 2007 and December 31, 2006	-	-
Common stock, \$0.01 par value, 240,000,000 shares authorized; 94,585,449 issued and outstanding at December 31, 2007 and 93,284,934 issued and outstanding at December 31, 2006	946	933
Additional paid-in capital	147,327	145,827
Accumulated deficit	(147,527)	(153,062)
<b>Stockholders' equity (deficit)</b>	<b>746</b>	<b>(6,302)</b>

Total liabilities and stockholders' equity (deficit)	\$	15,012	\$	2,439
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*See accompanying notes to consolidated financial statements.*

**INSITE VISION INCORPORATED**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**

(in thousands, except per share amounts)	Year Ended December 31,		
	2007	2006	2005
Revenues:			
Licensing fee and milestone amortization	\$ 22,080	\$ 2	\$ 4
Royalties	701	-	-
Other product and service revenue	980	-	-
Total	23,761	2	4
Cost of revenues	982	28	14
Gross margin	22,779	(26)	(10)
Operating expenses:			
Research and development(a)	10,384	8,890	10,690
General and administrative(a)	6,760	6,182	4,510
Total	17,144	15,072	15,200
Income (loss) from operations	5,635	(15,098)	(15,210)
Interest (expense) and other income, net	(100)	(1,513)	(5)
Net income (loss)	\$ 5,535	\$ (16,611)	\$ (15,215)
Net income (loss) per share:			
Earnings (loss) per share - basic	\$ 0.06	\$ (0.19)	\$ (0.21)
Earnings (loss) per share - diluted	\$ 0.06	\$ (0.19)	\$ (0.21)
Weighted average shares used in per-share calculation:			
- Basic	94,168	88,339	72,647
- Diluted	100,110	88,339	72,647
(a) Includes the following amounts related to stock based compensation:			
Research and development	\$ 282	\$ 245	\$ -
General and administrative	719	565	-

*See accompanying notes to consolidated financial statements.*

**INSITE VISION INCORPORATED**  
**CONSOLIDATED STATEMENTS OF STOCKHOLDER' EQUITY (DEFICIT)**

	<u>Preferred Stock</u>		<u>Common Stock</u>		Additional	Notes Receivable from	Retained Earnings (Accumulated	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
(in thousands, except per share amounts)					Paid-in-Capital	Stockholders	Deficit)	(Deficit)
<b>Balances, December 31, 2004</b>	-	\$ -	62,381,808	\$ 624	\$ 124,400	\$ (187)	\$ (121,236)	3,601
Issuance costs related to 2004 private placement	-	-	-	-	(262)	-	-	(262)
Issuance of common stock from exercise of options and employee stock purchase plan	-	-	65,647	-	33	-	-	33
Issuance of common stock from exercise of warrants	-	-	803,725	8	495	-	-	503
Issuance of common stock from private placement	-	-	16,363,626	164	7,978	-	-	8,142
Non-employee stock compensation	-	-	-	-	14	-	-	14
Loan payment from stockholder	-	-	-	-	-	19	-	19
Issuance of warrants in connection with private placement of notes payable	-	-	-	-	620	-	-	620
Net loss	-	-	-	-	-	-	(15,215)	(15,215)
<b>Balances, December 31, 2005</b>	-	-	79,614,806	796	133,278	(168)	(136,451)	(2,545)
Issuance of common stock from exercise of options and employee stock purchase plan	-	-	203,920	2	131	-	-	133
Issuance of common stock from exercise of warrants	-	-	8,676,132	87	5,539	-	-	5,626
Issuance of common stock from private placement	-	-	4,790,076	48	5,762	-	-	5,810

Employee stock compensation	-	-	-	-	804	-	-	804
Non-employee stock compensation	-	-	-	-	6	-	-	6
Loan payment from stockholder	-	-	-	-	-	168	-	168
Issuance of warrants in connection with private placement of notes payable	-	-	-	-	307	-	-	307
Net loss	-	-	-	-	-	-	(16,611)	(16,611)
<b>Balances, December 31, 2006</b>	-	-	93,284,934	933	145,827	-	(153,062)	(6,302)
Issuance of common stock from exercise of options and employee stock purchase plan	-	-	159,017	2	107	-	-	109
Issuance of common stock from exercise of warrants, net of issuance costs	-	-	1,141,498	11	392	-	-	403
Employee stock compensation	-	-	-	-	979	-	-	979
Non-employee stock compensation	-	-	-	-	22	-	-	22
Net income	-	-	-	-	-	-	5,535	5,535
<b>Balances, December 31, 2007</b>	-	\$ -	94,585,449	\$ 946	\$ 147,327	\$ -	(147,527)	\$ 746

See accompanying notes consolidated financial statements.

**INSITE VISION INCORPORATED**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(in thousands)

	Year Ended December 31,		
	2007	2006	2005
<b>OPERATING ACTIVITIES:</b>			
Net income (loss)	\$ 5,535	\$ (16,611)	\$ (15,215)
Adjustment to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	236	97	57
Gain on sale of assets	(1)	-	(4)
Amortization of deferred debt issuance costs	22	809	-
Accretion of debt discount	-	798	-
Stock-based compensation	1,001	810	14
Changes in operating assets and liabilities:			
Accounts receivable	(719)	-	-
Prepaid expenses and other current assets	(553)	(697)	(9)
Accounts payable	1,819	(1,564)	1,367
Accrued interest	(702)	699	-
Deferred revenue	10,145	-	-
Accrued liabilities	481	(786)	380
Accrued compensation and related expense, and other current liabilities	360	216	46
Net cash provided by (used in) operating activities	<u>17,624</u>	<u>(16,229)</u>	<u>(13,364)</u>
<b>INVESTING ACTIVITIES:</b>			
Purchase of property and equipment	(1,013)	(322)	(236)
Proceeds from sale of asset	1	-	4
Restricted cash decrease	-	-	95
Net cash used in investing activities	<u>(1,012)</u>	<u>(322)</u>	<u>(137)</u>
<b>FINANCING ACTIVITIES:</b>			
Issuance of common stock from exercise of options, employee purchase plan and warrants, net of issuance costs	512	5,759	536
Issuance of common stock from private placement, net of issuance costs	-	5,810	8,142
Issuance costs related to 2004 equity private placement	-	-	(262)
Note payment received from stockholder	-	168	19
Issuance of short-term notes payable, net of issuance costs	-	1,783	3,815
Repayments of borrowings	(6,300)	-	-
Payments of notes payable to related parties	(266)	-	(73)
Payment of capital lease obligation	(12)	(10)	-
Net cash (used in) provided by financing activities	<u>(6,066)</u>	<u>13,510</u>	<u>12,177</u>
Net increase (decrease) in cash and cash equivalents	10,546	(3,041)	(1,324)
Cash and cash equivalents at beginning of period	986	4,027	5,351
Cash and cash equivalents at end of period	<u>\$ 11,532</u>	<u>\$ 986</u>	<u>\$ 4,027</u>
<b>Supplemental disclosure of cash flow information:</b>			
Cash paid:			
Interest	<u>\$ 809</u>	<u>\$ 16</u>	<u>\$ 2</u>
Income taxes	<u>\$ 1</u>	<u>\$ 1</u>	<u>\$ 1</u>
Non-cash investing and financing activities:			

Issuance of warrants to lenders in connection with notes payable	\$	-	\$	307	\$	491
Issuance of warrants to placement agent in connection with notes payable	\$	-	\$	-	\$	129
Acquisition of property and equipment through capital lease	\$	-	\$	71	\$	-

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*See accompanying notes to consolidated financial statements.*

## InSite Vision Incorporated

Notes to Consolidated Financial Statements  
December 31, 2007

### 1. Summary of Significant Accounting Policies

Basis of Presentation. The accompanying consolidated financial statements include the accounts of InSite Vision, Inc. and its wholly-owned subsidiaries. InSite Vision (the “Company” or “InSite Vision”) operates in one segment and is focused on developing drugs and drug delivery systems principally for ophthalmic indications. All transactions have been eliminated between the subsidiaries and the Company.

#### Reclassifications

Certain other prior year balance sheet and cash flow amounts have been reclassified to conform to the current financial statement presentation. These reclassifications had no impact on previously reported results of operations or stockholders’ equity.

#### Significant Accounting Policies and Use of Estimates

Use of Estimates. The preparation of financial statements in conformity with generally accepted accounting principles in the United States of America requires the Company to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from those estimates.

Cash and cash equivalents. The Company considers all highly liquid investments with maturities of 90 days or less from the date of purchase to be cash equivalents.

Accounts receivable. Accounts Receivable represent amounts due to the Company from its licensees, Inspire and Shin Poong. The Company has not recorded a bad debt allowance related to these accounts receivable as the amounts are reasonably expected to be collected. The need for a bad debt allowance is evaluated each reporting period based on our assessment of the collectibility of the amounts.

Prepaid deal expenses, Prepaid expenses and other current assets. At December 31, 2007, prepaid deal expenses included \$538,000 of expenses incurred related to the financing completed in February 2008. See Note 15, “Subsequent Event” for further discussion of this transaction. At December 31, 2006, prepaid expenses included a receivable from the FDA of the \$767,000. This receivable represents the filing fee the Company paid in June 2006 when it filed its AzaSite New Drug Application. The FDA subsequently determined the fee would be waived and it was refunded to the Company.

Inventory. The Company’s inventories are stated at the lower of cost or market. The cost of the inventory is based on the first-in first-out method. If the cost of the inventory exceeds the expected market value, a provision is recorded for the difference between cost and market.

Property and Equipment. Property and equipment is stated at cost, less accumulated depreciation and amortization. Depreciation of property and equipment is provided over the estimated useful lives of the respective assets, which range from three to five years, using the straight-line method. Leasehold improvements and property acquired under capital lease are amortized over the lives of the related leases or their estimated useful lives, whichever is shorter, using the straight-line method. Depreciation and amortization expense for the years ended December 31, 2007, 2006 and 2005 were \$236,000, \$97,000 and \$57,000, respectively.

Additionally, the Company records impairment losses on long-lived assets used in operations when events and circumstances indicate that the assets might be impaired and the undiscounted cash flows estimated to be generated by those assets are less than the carrying amounts of those assets. No such impairments have been recorded to date.

The costs of repairs and maintenance are expensed as incurred.

Revenue Recognition. The Company recognizes revenue in accordance with Securities and Exchange Commission Staff Accounting Bulletin No. 104, Revenue Recognition, or SAB 104. SAB 104 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectibility is reasonably assured. Arrangements with multiple elements are accounted for in accordance with Emerging Issues Task Force, or EITF, Issue No. 00-21, Revenue Arrangements with Multiple Deliverables. The Company analyzes our multiple element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting in accordance with EITF 00-21. The Company's revenues are primarily related to licensing agreements, and such agreements may provide for various types of payments, including upfront payments, research funding and related fees during the term of the agreement, milestone payments based on the achievement of established development objectives, licensing fees, and royalties on product sales.

Upfront, non-refundable payments under licensing agreements are recorded as deferred revenues once received and recognized ratably over the period related activities are performed. Revenues from non-refundable milestones are recognized when the earnings process is complete and the payment is reasonably assured. Non-refundable milestone payments related to arrangements under which the Company has continuing performance obligations are recognized ratably over the period related activities are performed.

Revenue related to contract research services is recognized when the services are provided and collectibility is reasonable assured.

The Company receives royalties from licensees based on third-party sales. The royalties are recorded as earned in accordance with the contract terms when third-party results are reliably measured and collectibility is reasonably assured.

Revenues related to the sales of the Company's OcuGene glaucoma genetic test were recognized when all related services had been rendered and collectibility was reasonably assured.

Cost of revenues. The Company recognizes the cost of inventory shipped and other costs related to the Company's OcuGene glaucoma genetic test when they are incurred.

Research and Development (R&D) Expenses. R&D expenses include salaries, benefits, facility costs, services provided by outside consultants and contractors, administrative costs and materials for the Company research and development activities. The Company also funds research at a variety of academic institutions based on agreements that are generally cancelable. The Company recognizes such costs as they are incurred.

The Company accrues and expenses the costs for clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with contract research organizations and clinical trial sites. The Company determines the estimates through discussions with internal clinical personnel and external service providers as to progress or stage of completion of trials or services and the agreed upon fee to be paid for such services. Costs of setting up clinical trial sites for participation in the trials are expensed immediately as research and development expenses. Clinical trial site costs related to patient enrollment are accrued as patients are entered into the trial.

General and Administrative (G&A) Expenses. G&A expenses include salaries, benefits, facility costs, services provided by outside consultants and contractors, advertising and marketing, investor relations, financial reporting, materials and other expenses related to general corporate and sales and marketing activities. The Company recognizes such costs as they are incurred.

Stock-Based Compensation. Our stock-based compensation programs consist of stock options granted to employees as well as our employee stock purchase plan, or ESPP.

Effective January 1, 2006, the Company adopted the provisions of Statement of Financial Accounting Standards (“SFAS”) No. 123 (revised 2004) “Share-Based Payment” (“SFAS No. 123 (R)”). SFAS No. 123 (R) establishes accounting for stock-based awards exchanged for employee services. Accordingly, stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as expense over the requisite service period. All of the Company’s stock compensation is accounted for as an equity instrument. The Company previously applied Accounting Principles Board (“APB”) Opinion No. 25, “Accounting for Stock Issued to Employees,” and related interpretations and provided the required pro forma disclosures of SFAS No. 123, “Accounting for Stock-Based Compensation”.

Upon adoption of SFAS No. 123(R), the Company elected the alternative transition method for calculating the tax effects of stock-based compensation pursuant to SFAS No. 123(R). The alternative transition method provides a simplified method to establish the beginning balance of the additional paid-in capital pool, or APIC Pool, related to the tax effects of employee stock-based compensation, and to determine the subsequent impact on the APIC Pool and consolidated statements of cash flows of the tax effects of employee stock-based compensation awards that are outstanding upon adoption of SFAS No. 123(R).

Consistent with prior years, the Company uses the “with and without” approach as described in Emerging Issues Task Force Topic No. D-32 in determining the order in which its tax attributes are utilized. The “with and without” approach results in the recognition of the windfall stock option tax benefits after all other tax attributes have been considered in the annual tax accrual computation. SFAS No. 123(R) prohibits the recognition of a deferred tax asset for an excess tax benefit that has not yet been realized. As a result, the Company will only recognize a benefit from stock-based compensation in paid-in capital if an incremental tax benefit is realized after all other tax attributes currently available to it have been utilized. In addition, the Company has elected to account for the indirect benefits of stock-based compensation on items such as the alternative minimum tax, the research tax credit or the domestic manufacturing deduction through the consolidated statements of operations rather than through paid-in capital. See Note 9, “Employee Stock-Based Compensation” for further discussion of employee stock-based compensation.

Prior to the Adoption of SFAS No. 123(R)

Prior to the adoption of SFAS No. 123(R), the Company provided the disclosures required under SFAS No. 123, “Accounting for Stock-Based Compensation,” as amended by SFAS No. 148, “Accounting for Stock-Based Compensation — Transition and Disclosures.”

The fair value for these options was estimated at the date of grant using a Black-Scholes option pricing model with the following weighted-average assumptions for 2005, risk-free interest rates ranging from 4.3% to 4.4%; volatility factors for the expected market price of our common stock of 103%; expected life of 4 years; and an expected dividend rate of 0%.

The following table illustrates the effect on net loss and net loss per share as if the Company had applied the fair value recognition provisions of SFAS 123 to stock-based employee and director compensation (in thousands, except per share amounts):

	Year Ended December 31, 2005
Net loss - as reported	\$ (15,215)
Deduct: Total stock-based employee compensation expense determined under fair value method for all awards	(524)
Net loss-pro forma	\$ (15,739)
Loss per share:	
Basic and diluted-as reported	\$ (0.21)
Basic and diluted-pro forma	\$ (0.22)

Accounting for Stock Options and Warrants Exchanged for Services. The Company issues stock options and warrants to consultants of the Company in exchange for services. The Company has valued these options and warrants using the Black-Scholes option pricing model in accordance with the Emerging Issues Task Force (EITF) Consensus No. 96-18, "Accounting for Equity Investments that are Issued to Other Than Employees for Acquiring or in Conjunction with Selling Goods, or Services," at each reporting period and has recorded charges to operations over the vesting periods of the individual stock options or warrants. Such charges amounted to approximately \$22,000, \$6,000 and \$14,000 during the years ended 2007, 2006 and 2005, respectively.

Income (Loss) per Share. Basic and diluted net income (loss) per share information for all periods is presented under the requirement of SFAS No. 128, "Earnings per Share." Basic net loss per share has been computed using the weighted-average number of common shares outstanding during the period. Dilutive net loss per share is computed using the sum of the weighted-average number of common shares outstanding and the potential number of dilutive common shares outstanding during the period. Potential common shares consist of the shares issuable upon exercise of stock options and warrants. Potentially dilutive securities have been excluded from the computation of diluted net loss per share in 2006 and 2005 as their inclusion would be antidilutive.

The following table sets forth the computation of basic and diluted net loss per share:

(in thousands, except per share data)	Year Ended December 31,		
	2007	2006	2005
<b>Numerator:</b>			
Net income (loss)	\$ 5,535	\$ (16,611)	\$ (15,215)
<b>Denominator:</b>			
Weighted-average shares outstanding	94,168	88,339	72,647
<b>Effect of dilutive securities:</b>			
Stock options and warrants	5,942	-	-
Weighted-average shares outstanding for diluted income(loss)	100,110	88,339	72,647
<b>Net income (loss) per share:</b>			
Basic	\$ 0.06	\$ (0.19)	\$ (0.21)
Diluted	\$ 0.06	\$ (0.19)	\$ (0.21)

For the year ended 2006 and 2005, due to the loss applicable to common stockholders, loss per share is based on the weighted average number of common shares only, as the effect of including equivalent shares from stock options and warrants would be anti-dilutive. At December 31, 2007, 2006 and 2005, 1,016,957, 23,412,320 and 30,253,869 options and warrants were excluded from the calculation of diluted earnings per share because the effect was anti-dilutive.

Accounting for Materials Purchased for Research and Development. The Company expenses materials for research and development activities when the obligation for the items is incurred.

Key Suppliers. The Company is dependent on single or limited source suppliers for certain materials used in its research and development and commercial activities. The Company has generally been able to obtain adequate supplies of these components. However, an extended interruption in the supply of these components currently obtained from single or limited source suppliers could adversely affect the Company's research and development and commercial efforts.

Income Taxes. Income tax expense has been provided using the liability method. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities as measured by the enacted tax rates that will be in effect when these differences reverse. The Company provides a valuation allowance against net deferred tax assets if, based upon the available evidence, it is not more likely than not that the deferred tax assets will be realized.

Effective January 1, 2007, the Company adopted the provisions of Financial Accounting Standard Board, Financial Interpretation No. 48, Accounting for Uncertainty in Income Taxes — an interpretation of FASB Statement No. 109, or FIN 48. FIN 48 specifies how tax benefits for uncertain tax positions are to be recognized, measured and derecognized in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim-period guidance, among other provisions.

At the date of adoption of FIN 48, the Company had no unrecognized tax benefits and expected no significant changes in unrecognized tax benefits in the next 12 months.

The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense. To date, there have been no interest or penalties charged to the Company in relation to the underpayment of income taxes.

Significant Customers and Risk. All revenues recognized and deferred in 2007 were from our two AzaSite licensees. The Company is entitled to receive royalty revenue from net sales of AzaSite under the terms of its agreements with Inspire and Shin Poong, and accordingly, all trade receivables are concentrated with these parties. Due to the nature of these agreements, these parties have significant influence over the commercial success of AzaSite.

Credit Risk. Financial instruments that potentially subject the Company to significant concentrations of credit risk consist principally of cash and cash equivalents. The Company's cash and cash equivalents are primarily deposited in demand accounts with one financial institution.

Risks from Third Party Manufacturing Concentration. The Company relies on a single source manufacturer for each of its product candidates and on a single source manufacturer for the active pharmaceutical ingredient in its product candidates. Inspire is responsible for the manufacturing of AzaSite and relies on single source manufacturer for the product and on a single source manufacturer for the active pharmaceutical ingredient in the product. Accordingly, delays in the manufacture of the product or product candidate could adversely impact the marketing of the Company's product or the development of the Company's product candidates. Furthermore, the Company has no control over the manufacture of products for which it is entitled to receive revenue and the overall product supply chain.

#### Recent Accounting Pronouncements.

In September 2006, the Financial Accounting Standards Board ("FASB") issued SFAS No. 157, "Fair Value Measurements" ("SFAS No. 157"). SFAS No. 157 provides guidance for using fair value to measure assets and liabilities. It also responds to investors' request for expanded information about the extent to which companies measure assets and liabilities at fair value, the information used to measure fair value, and the effect of fair valued measurements on earnings. SFAS No. 157 applies whenever standards require (or permit) assets or liabilities to be measured at fair value, and does not expand the use of fair value in any new circumstances. SFAS No. 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007, and interim periods within those fiscal years, with early adoption permitted, except for the impact of FASB Staff Position (FSP) 157-2. FSP 157-2 deferred the adoption of SFAS 157 for non financial assets and liabilities until years ended after November 15, 2008. The Company must adopt these requirements no later than the first quarter of 2008. The Company does not anticipate the adoption of SFAS No. 157 will have a material effect on its consolidated financial position, results of operations or liquidity.

In February 2007, the FASB issued SFAS No. 159, “The Fair Value Option for Financial Assets and Financial Liabilities — Including an amendment of FASB Statement No. 115” (“SFAS No. 159”). SFAS No. 159 expands the use of fair value accounting but does not affect existing standards that require assets or liabilities to be carried at fair value. Under SFAS No. 159, a company may elect to use fair value to measure accounts and loans receivable, available-for-sale and held-to-maturity securities, equity method investments, accounts payable, guarantees and issued debt. Other eligible items include firm commitments for financial instruments that otherwise would not be recognized at inception and non-cash warranty obligations where a warrantor is permitted to pay a third party to provide the warranty goods or services. If the use of fair value is elected, any upfront costs and fees related to the item must be recognized in earnings and cannot be deferred (e.g., debt issue costs). The fair value election is irrevocable and generally made on an instrument-by-instrument basis, even if a company has similar instruments that it elects not to measure based on fair value. At the adoption date, unrealized gains and losses on existing items for which fair value has been elected are reported as a cumulative adjustment to beginning retained earnings. Subsequent to the adoption of SFAS No. 159, changes in fair value are recognized in earnings. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. The Company is currently determining whether fair value accounting is appropriate for any of its eligible items and cannot estimate the impact, if any, that SFAS No. 159 will have on its consolidated financial position, results of operations or liquidity.

In November 2007, the FASB ratified EITF Issue No. 07-1, “Accounting for Collaborative Agreements Related to the Development and Commercialization of Intellectual Property” (“EITF Issue No. 07-1”). EITF Issue No. 07-1 defines collaborative agreements as a contractual arrangement in which the parties are active participants to the arrangement and are exposed to the significant risks and rewards that are dependent on the ultimate commercial success of the endeavor. Additionally, it requires that revenue generated and costs incurred on sales to third parties as it relates to a collaborative agreement be recognized as gross or net based on EITF Issue No. 99-19, “Reporting Revenue Gross as a Principal versus Net as an Agent.” It also requires payments between participants to be accounted for in accordance with already existing generally accepted accounting principles, unless none exist, in which case a reasonable, rational, consistent method should be used. EITF Issue No. 07-1 is effective for fiscal years beginning after December 15, 2008 for all collaborative arrangements existing as of that date, with retrospective application to all periods. The Company does not anticipate the adoption of EITF Issue No. 07-1 will have a material effect on its financial position, results of operations or liquidity.

In June 2007, the FASB ratified EITF Issue No. 07-3, “Accounting for Non-Refundable Payments for Goods or Services Received for Use in Future Research and Development Activities” (“EITF Issue No. 07-3”). EITF Issue No. 07-3 requires that nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities be deferred and capitalized and recognized as an expense as the goods are delivered or the related services are performed. EITF Issue No. 07-3 is effective, on a prospective basis, for fiscal years beginning after December 15, 2007. The Company does not anticipate the adoption of EITF Issue No. 07-3 will have a material effect on its consolidated financial position, results of operations or liquidity.

In December 2007, the FASB issued SFAS No. 141(Revised 2007), “Business Combinations” (“SFAS No. 141(R)”). SFAS No. 141(R) changes the requirements for an acquirer’s recognition and measurement of the assets acquired and liabilities assumed in a business combination, including the treatment of contingent consideration, pre-acquisition contingencies, transaction costs, in-process research and development and restructuring costs. In addition, under SFAS No. 141(R), changes in an acquired entity’s deferred tax assets and uncertain tax positions after the measurement period will impact income tax expense. This statement is effective for the Company with respect to business combination transactions for which the acquisition date is after December 31, 2008.

In December 2007, the FASB issued SFAS No. 160, “Non-controlling Interests in Consolidated Financial Statements (an amendment of Accounting Research Bulletin No. 51)” (“SFAS No. 160”). SFAS No. 160 requires that non-controlling (minority) interests be reported as a component of equity, that net income attributable to the parent and to the non-controlling interest be separately identified in the income statement, that changes in a parent’s ownership interest while the parent retains its controlling interest be accounted for as equity transactions, and that any retained non-controlling equity investment upon the deconsolidation of a subsidiary be initially measured at fair value. This statement is effective for fiscal years beginning after December 31, 2008, and shall be applied prospectively. However, the presentation and disclosure requirements of SFAS No. 160 are required to be applied retrospectively for all periods presented. The retrospective presentation and disclosure requirements of this statement will be applied to any prior periods presented in financial statements for the fiscal year ending December 31, 2009, and later periods during which the Company had a consolidated subsidiary with a non-controlling interest. As of December 31, 2007, the Company does not have any consolidated subsidiaries in which there is a non-controlling interest.



## 2. License Agreements

In December 2007, the Company entered into an international licensing and distribution agreement for AzaSite with Shin Poong Pharm, Seoul, South Korea. Under the terms of the agreement, the Company granted exclusive rights to Shin Poong to commercialize AzaSite for ocular bacterial infection in South Korea. Shin Poong will also be responsible for securing approval of AzaSite in South Korea. In exchange, Shin Poong will pay the Company upfront and regulatory milestone payments as well as a double-digit royalty on net sales of AzaSite in South Korea, if approved by regulatory authorities. The Company will be responsible for providing manufactured products at cost to Shin Poong.

On February 15, 2007, the Company entered into a license agreement for AzaSite<sup>TM</sup> with Inspire under which the Company licensed to Inspire exclusive development and commercialization rights in the United States and Canada, for topical anti-infective products containing azithromycin as the sole active ingredient for human ocular or ophthalmic indications. The Company also granted Inspire an exclusive sublicense under the Pfizer patent rights the Company has licensed under the Pfizer License discussed below. Inspire has the right to grant sublicenses under the terms of the Inspire License.

Inspire paid the Company an upfront license fee of \$13 million on February 15, 2007 and on May 11, 2007 paid an additional \$19 million upon regulatory approval by the U.S. FDA. Inspire also pays the Company a royalty on net sales of AzaSite in the United States and Canada. The royalty rate is 20% of net sales in the first two years of commercialization and 25% thereafter. Inspire is obligated to pay the Company royalties under the Inspire License for the longer of (i) eleven years from the launch of the first product, or (ii) the period during which a valid claim under a patent exists. For five years after the first year of commercial sale, Inspire will pay the Company certain tiered minimum royalties. The royalties discussed above are subject to certain reductions in the event of patent invalidity, generic competition, uncured material breach or in the event that Inspire is required to pay license fees to third parties for the continued use of AzaSite.

The Company also entered into a supply agreement, or the Supply Agreement, with Inspire on February 15, 2007 for the active pharmaceutical ingredient azithromycin. The Company had previously entered into a third-party supply agreement for the production of such active ingredient.

The Company is recognizing the upfront license fee and milestone payment totaling \$32 million ratably over the period that the Company is required to continue to provide services under the license agreement, which is expected to be until the second quarter of 2008, under the contingency-adjusted performance model of revenue recognition. During the year ended December 31, 2007, the Company recognized \$22.1 million of the license fee and milestone payment as revenue.

In August 2007, Inspire commercially launched AzaSite in the United States. Correspondingly, during the year ended December 31, 2007, the Company recognized \$701,000 of royalties related to sales of AzaSite by Inspire. Additionally, during the period ended December 31, 2007, the Company recognized \$980,000 of revenue from Inspire for the sales of the active ingredient, azithromycin, under the Supply Agreement, sales of AzaSite inventory and for contract services provided.

On February 15, 2007, the Company entered into a worldwide, exclusive, royalty-bearing license agreement with Pfizer Inc. under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus<sup>TM</sup> (the "Pfizer License"). Under the Pfizer License, the Company is required to pay Pfizer a low single digit royalty based on net sales of the licensed products and to use reasonable commercial efforts to seek regulatory approval for and market licensed products. The Pfizer License provides the Company the right to grant sublicenses thereunder, subject to Pfizer's prior approval, which approval shall not be unreasonably withheld. Pfizer approved the sublicense granted to Inspire. Based on the royalty report provided by Inspire, for the period ended December 31, 2007, the Company recorded third-party royalties of \$122,000 due primarily under the Pfizer License which was recorded in cost revenues within the consolidated statements of operations.

### 3. Restricted Cash

In December 2005, the Company reserved approximately \$75,000 related to a letter of credit issued as collateral for a capital lease for a telephone system which was installed and initiated in the first quarter of 2006. The Company anticipates that the requirement for this restricted cash will be eliminated in 2008.

### 4. Accounts Receivable

Accounts receivable primarily represent amounts due to the Company from Inspire and Shin Poong. The Company has not recorded a bad debt allowance related to these accounts receivable as the amounts were deemed collectible at December 31, 2007. The need for a bad debt allowance is evaluated each reporting period based on our assessment of the collectibility of the amounts.

### 5. Short-term Notes Payable, Secured

In 2005 and 2006, the Company issued a total of \$6,300,000 of short-term senior secured notes payable and warrants to purchase 1,260,000 shares of Common Stock at an exercise price of \$0.82 per share. The Company also issued warrants to purchase 200,000 shares of Common Stock at an exercise price of \$0.82 per share to the placement agent engaged for such financing.

These notes, and the senior secured notes described in Note 11, were secured by a lien on all of the assets of the Company, including the Company's intellectual property. These notes bore interest at a rate of ten percent (10%) and had an original maturity date of June 30, 2006, which maturity date was extended for an additional six months at an interest rate of twelve percent (12%). In February 2007, these notes were repaid in full.

### 6. Commitments and Contingencies

At December 31, 2007, the Company had purchase commitments and contractual obligations of approximately \$25.2 million, primarily related to its AzaSite Plus Phase 3 study, future royalty payments, minimum license fees and consultant costs. These purchase commitments and contractual obligations are reflected in the Company's financial statements once the related goods or services have been received or payments related to the obligations become due.

Capital lease obligations represent the present value of future rental payments under capital lease agreements for telephones and telephone equipment. At December 31, 2007 and 2006 the Company had \$71,000 of capital leased equipment with accumulated depreciation of \$23,000 and \$7,000, respectively.

Future minimum payments under capital leases are as follows:

Year Ending December 31,	Capital Leases
2008	\$ 17,661
2009	17,661
2010	17,661
2011	4,750
2012	-
Total minimum lease payments	57,733
Amount representing interest	(8,713)
Present value of net minimum lease payment	49,020
Current Portion, in other current liabilities	(13,352)
Long-term portion	\$ 35,668

The Company conducts its operations from leased facilities in Alameda, California under non-cancelable operating lease agreements that expire in 2013. Lease payments include rent and the Company's pro-rata share of operation expenses. For accounting purposes, the Company is amortizing all rent payments ratably over the life of the lease. Future minimum lease payments under this lease and a reconciliation of rent expense to rent paid is in the table below. Rent expense for the year ended December 31, 2007, 2006 and 2005, was \$695,000, \$706,000, and \$719,000, respectively.

Year Ending December 31,	Operating Lease Cash Payments Required
2008	\$ 730,824
2009	754,132
2010	775,175
2011	798,483
2012	821,790
2013 and thereafter	847,528
<b>Total minimum lease payments</b>	<b>\$ 4,727,932</b>

## 7. Income Taxes

The provision of income taxes is determined using an estimated annual effective tax rate. The Company's effective tax rate may be subject to fluctuations during the year as new information is obtained, which may affect the assumptions management uses to estimate the annual effective tax rate. The effective income tax rate was 0.0% for the period ended December 31, 2007 due to the use of previously generated net operating losses. There was no provision for income taxes for the period ended December 31, 2006 and 2005 due to the Company's net operating losses.

Significant components of the Company's deferred tax assets for federal and state income taxes as of December 31, 2007 and 2006 are as follows (in thousands):

	2007	2006
Deferred tax assets:		
Net operating loss carryforwards	\$ 37,786	\$ 40,614
Tax credit carryforwards	5,637	6,456
Capitalized research and development	10,208	12,263
Depreciation	381	398
Other	300	95
Total deferred tax assets	\$ 54,312	59,826
Valuation allowance	(54,312)	(59,826)
Net deferred tax assets	\$ -	\$ -

The valuation allowance decreased by \$5.5 million, during the year ended December 31, 2007 and increased by \$6.6 million and \$4.4 million during the years ended December 31, 2006 and 2005, respectively.

At December 31, 2007, the Company had net operating loss carryforwards for federal income tax purposes of approximately \$98.8 million, which expire in the years 2007 through 2026 and federal tax credits of approximately \$2.3 million, which expire in the years 2007 through 2026. At December 31, 2007, the Company also has net operating loss carryforwards for state income tax purposes of approximately \$70.0 million which expire in the years 2007 through 2016, and state research and development tax credits of approximately and \$3.3 million which carryforward indefinitely.

Utilization of the Company's federal and state net operating loss carryforwards and research and development tax credits are subject to an annual limitation against taxable income in future periods due to the ownership change limitations provided by the Internal Revenue Code of 1986. As a result of this annual limitation, a significant portion of these carryforwards will expire before ultimately becoming available for offset against taxable income. Additional losses and credits will be subject to limitation if the Company incurs

another change in ownership in the future.

The Company files income tax returns in the U.S. federal and California jurisdictions. The Company is no longer subject to tax examinations for years before 2005 for federal returns and 2004 for California returns, except to the extent that it utilizes net operating losses or tax credit carryforwards that originated before those years. The Company is not currently under audit by any major tax jurisdiction nor has it been in the past.

## 8. Common Stockholders' Equity (Deficit)

In 2007, the Company received approximately \$403,000, net of approximately \$10,000 of fees, from the exercise of warrants to purchase 568,211 shares of Common Stock issued as part of private placements. In addition, warrants to purchase 921,328 shares of Common Stock were exercised as cashless warrant exercises resulting in the issuance of 573,287 net shares. The Company also received approximately \$70,000 from the exercise of 96,192 options issued to employees and approximately \$39,000 from the issuance of 62,825 shares acquired under the employee stock purchase plan.

In 2006, the Company issued 8,676,132 shares of Common Stock and received approximately \$5,626,000, net of approximately \$162,000 of fees, from the exercise of warrants to purchase 9,207,452 shares of Common Stock. The following table summarizes the 2006 exercises by the transaction that the warrants related to:

Warrants issued as part of:	Exercise Price	Net Cash Received	Fees Incurred	Warrants Exercised	Shares of Common Stock Issued
March 2004 private placement	\$ 0.75	\$ 5,256,000	\$ 162,000	7,223,763	7,223,763
Placement agent warrants related to the March 2004 private placement, cashless exercise	\$ 0.55	-	-	29,077	17,719
May 2005 private placement	\$ 0.63	345,000	-	545,451	545,451
May 2005 private placement, cashless exercise	\$ 0.63	-	-	436,361	274,074
Legal settlement	\$ 0.50	-	-	922,800	565,125
2003 services provided	\$ 0.50	25,000	-	50,000	50,000
<b>Total</b>		<b>\$ 5,626,000</b>	<b>\$ 162,000</b>	<b>9,207,452</b>	<b>8,676,132</b>

The following table shows the detail of outstanding warrants as of December 31, 2007. All of the outstanding warrants, except for those issued in March and June, 2004, with an exercise price of \$0.75, have cashless exercise provisions.

Date Issued	Warrants Shares	Exercise Price	Expiration Date	Cash if Converted
September 22, 2003	81,967	\$ 0.61	September 21, 2008	\$ 50,000
March 26, 2004	989,401	0.75	March 25, 2009	742,051
June 14, 2004	7,414,569	0.75	June 13, 2009	5,560,927
June 14, 2004	351,640	0.55	June 13, 2009	193,402
May 26, 2005	3,818,175	0.63	May 25, 2010	2,414,996
May 26, 2005	366,136	0.63	May 25, 2010	231,581
December 30, 2005	860,000	0.82	December 29, 2010	705,200
December 30, 2005	100,000	0.82	December 29, 2010	82,000
January 11, 2006	400,000	0.82	January 10, 2011	328,000

August 16, 2006	<u>958,015</u>	1.51	August 15, 2011	<u>1,446,603</u>
Total	<u>15,339,903</u>			<u>\$ 11,754,760</u>
Weighted-average exercise price per share				<u>\$ 0.77</u>

In August 2006, the Company received, net of placement fees, approximately \$5.8 million from a private placement pursuant to which it issued 4,790,076 shares of Common Stock and warrants to purchase 958,015 shares of Common Stock at an exercise price of \$1.51 per share. These warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 5.1%, volatility of 78.8% and an expected life of 5 years, resulting in the recording of a stock issue cost of approximately \$1.0 million for the warrants issued to the investors.

On May 26, 2005, the Company received, net of placement fees, approximately \$8.1 million from a private placement pursuant to which it issued 16,363,626 shares of Common Stock and warrants to purchase 4,909,077 shares of Common Stock at an exercise price of \$0.6325 per share. The Company also issued warrants to purchase 818,181 shares of Common Stock at an exercise price of \$0.6325 per share to the placement agent engaged for such financing. These warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 2.32%, volatility of 1.0435 and an expected life of 5 years, resulting in the recording of a stock issue cost of approximately \$2.4 million for the warrants issued to the investors in the private placement and \$0.4 million for the warrants issued to the placement agent.

In 2005, a final award was issued by the arbitrator of a legal action brought against the Company by Bristol Investment Group in regards to placement agent fees related to a 2004 private placement. As a result of the award, the Company paid and recorded a placement agent fee, including interest, of \$262,000. Bristol also received the right to purchase for \$922.80 a five-year, net-exercisable warrant to purchase 922,800 shares of our Common Stock at an exercise price of \$0.50 per share. The warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 4.18%, volatility of 1.04 and an expected life of 5 years, resulting in the recording of a stock issue cost of approximately \$467,000. In January 2006, the warrants were exercised using the non-cash exercise provision in the warrant for a total of 565,125 shares of Common Stock.

In 2005, the Company received approximately \$308,000, from the exercise of warrants to purchase 410,206 shares of Common Stock issued as part of the March 2004 private placement. In December 2005, the Company received approximately \$145,000 from the exercise of warrants to purchase 268,519 shares of Common Stock issued in December 2003. In January 2005, the Company received approximately \$50,000 from the exercise of warrants to purchase 125,000 shares of Common Stock issued in November 2003. In August 2005, the Company received approximately \$10,000 from the exercise of an employee stock option to purchase 25,000 shares of Common Stock.

## 9. Employee Stock-based Compensation

Effective January 1, 2006, the Company adopted the provisions of SFAS No. 123(R), which supersedes our previous accounting under APB 25. SFAS No. 123 (R) establishes accounting for stock-based awards exchanged for employee services. Accordingly, stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as expense over the requisite service period. All of the Company's stock compensation is accounted for as an equity instrument.

The effect of recording stock-based compensation for the year ended December 31, 2007, 2006 and 2005 was as follows (in thousands):

	Year Ended December 31,		
	2007	2006	2005
Stock-based compensation expense by type of award:			
Employee stock options	\$ 936	\$ 780	\$ -
Employee stock purchase plan	43	24	-
Non-employee stock options	22	6	14
Total stock-based compensation	\$ 1,001	\$ 810	\$ 14

## Employee Stock-based Compensation

During the year ended December 31, 2007 and December 31, 2006, respectively, the Company granted options to purchase 1,071,001 and 1,628,200 shares of common stock with an estimated total grant date fair value of \$1.0 million and \$1.6 million. Based on the Company's historical experience of option pre-vesting cancellations and estimates of future forfeiture rates, the Company has assumed an annualized forfeiture rate of 10% for its options for all periods disclosed. Accordingly, of the \$1.0 million and \$1.6 million, the Company estimated that the stock-based compensation for the awards not expected to vest was \$0.2 million and \$0.3 million, respectively. During the year ended December 31, 2007 and December 31, 2006, the Company recorded employee stock-based compensation related to all stock options of \$936,000 and \$780,000, respectively.

As of December 31, 2007 and 2006, unrecorded deferred stock-based compensation balance related to stock options was \$1.8 million and \$1.8 million, respectively, and will be recognized over an estimate weighted-average amortization period of 2.3 years and 1.2 years, respectively.

### Valuation assumptions

The Company estimates the fair value of stock options using a Black-Scholes valuation model, consistent with the provisions of SFAS No. 123 (R), Securities and Exchange Commission Staff Accounting Bulletin No. 107 and the Company's prior period pro forma disclosures of net loss, including stock-based compensation (determined under a fair value method as prescribed by SFAS No. 123). The fair value of each option grant is estimated on the date of grant using the Black-Scholes option valuation model and the graded-vesting method with the following weighted-average assumptions:

	Year ended	
	December 31,	
	2007	2006
Risk-free interest rate	3.3% - 4.6%	4.4% -5.1%
Expected term(years)	5	5
Expected dividends	0.0%	0.0%
Volatility	74.8%	78.0%

The dividend yield of zero is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends. Expected volatility is based on the combination of historical volatility of the Company's common stock and the common stock of the Company's competitors, the expected moderation in future volatility over the period commensurate with the expected life of the options and other factors. The risk-free interest rates are taken from the Daily Federal Yield Curve Rates as of the grant dates as published by the Federal Reserve and represent the yields on actively traded Treasury securities for terms equal to the expected term of the options. The expected term calculation is based on the terms utilized by the Company's competitors, observed historical option exercise behavior and post-vesting forfeitures of options by the Company's employees.

## Equity Incentive Program

Prior to October 15, 2007, the Company granted options under a stock option plan adopted in 1994 and amended thereafter (the "1994 Plan"), that allowed for the granting of non-qualified stock options, incentive stock options and stock purchase rights to the Company's employees, directors, and consultants. On October 15, 2007, the Company's stockholders approved a new equity incentive plan, the 2007 Performance Incentive Plan (the "2007 Plan"), that provides for grants of options and other equity-based awards to the Company's employees, directors and consultants. The Company's authority to grant new awards under the 1994 Plan terminated upon stockholder approval of the 2007 Plan. Options granted under these plans expire 10 years after the date of grant and become exercisable at such times and under such conditions as determined by the Company's Board of Directors or a committee appointed by the Board (generally with 25% vesting after one year and the balance vesting on a daily basis over the next three years of service). Upon termination of the optionee's service, unvested options terminate, and vested options generally expire at the end of three months. Only nonqualified stock options have been granted under these plans to date. On January 1 of each calendar year during the term of the 2007 Plan, the shares of Common Stock available for issuance will be increased by the lesser of 2% of the total outstanding shares of Common Stock on December 31 of the preceding calendar year, or 3,000,000 shares. The followings is a summary of activity under these plans for the indicated periods:

	Number of shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2004	3,835,736	\$ 1.58	6.28	\$ 326
Granted	2,175,000	0.65		
Exercised	(25,000)	0.41		
Canceled	(430,746)	2.40		
Outstanding at December 31, 2005	5,554,990	\$ 1.15	7.24	\$ 639
Granted	1,628,200	1.52		
Exercised	(136,257)	0.68		
Canceled	(464,055)	2.01		
Outstanding at December 31, 2006	6,582,878	\$ 1.19	7.08	\$ 3,597
Granted	1,071,001	1.43		
Exercised	(96,192)	0.73		
Canceled	(553,832)	3.07		
Outstanding at December 31, 2007	7,003,855	\$ 1.09	6.84	\$ 349
Options vested and exercisable and expected to be exercisable at December 31, 2007			6.72	
	6,474,688	\$ 1.08		\$ 331
Options vested and exercisable at December 31, 2007	4,629,501	\$ 1.01	6.00	\$ 280

At December 31, 2007, the Company had 1,995,074 shares of Common Stock available for grant of issuance under its 2007 Plan. The weighted average grant date fair value of options granted during the years ended December 31, 2007, 2006 and 2005 were \$0.91, \$1.52 and \$0.65, respectively. The total intrinsic value of options exercised during the years ended December 31, 2007, 2006 and 2005 were \$75,000 and \$157,000 and \$2,000, respectively.

The following table summarizes information concerning outstanding and exercisable options as of December 31, 2007:

Range of Exercise Prices	Option Outstanding			Options Vested and Exercisable	
	Number Outstanding	Weighted-Average		Number Exercisable	Weighted-Average Exercise Price
		Contractual Life	Exercise Price		
\$0.41 - \$0.60	280,750	5.97	\$ 0.41	279,473	\$ 0.41

\$0.63 - \$0.63	1,958,829	7.26	0.63	1,399,899	0.63
\$0.64 - \$0.84	726,726	6.23	0.73	664,452	0.73
\$0.85 - \$0.93	830,510	6.49	0.89	667,790	0.90
\$1.02 - \$1.45	817,414	3.40	1.19	668,282	1.20
\$1.46 - \$1.46	20,001	9.25	1.46	10,002	1.46
\$1.50 - \$1.50	1,352,668	8.07	1.50	642,455	1.50
\$1.56 - \$1.59	719,707	9.30	1.59	8,167	1.56
\$1.63 - \$5.25	287,250	5.30	2.65	278,981	2.68
\$5.88 - \$5.88	10,000	2.73	5.88	10,000	5.88
	<u>7,003,855</u>	6.84	\$ 1.09	<u>4,629,501</u>	\$ 1.01

At December 31, 2006 and 2005 options to purchase 3,720,567 and 3,173,607 shares of common stock were exercisable at weighted-average exercise prices of \$1.25 and \$1.51, per share, respectively.

## Employee Stock Purchase Plans

The Company currently maintains an employee stock purchase plan, adopted in 1994 and amended thereafter (the “Purchase Plan”). The Purchase Plan operates in 24-month “offering periods” that are each divided into four six-month “purchase periods.” The Purchase Plan allows eligible employees to purchase Common Stock at 85% of the lower of the fair market value of the Common Stock on the first day of the applicable offering period or the fair market value of the Common Stock on the last day of the applicable purchase period. Purchases are limited to 10% of each employee’s eligible compensation, subject to certain Internal Revenue Service restrictions. All of the Company’s employees are eligible to participate in the Purchase Plan after certain service periods are met. The number of shares available for issuance under the Purchase Plan is automatically increased on the first trading day in January each calendar year, by an amount equal to 0.5% of the total number of shares of Common Stock outstanding on the last trading day in December in the immediately preceding calendar year, but in no event will any such annual increase exceed 125,000 shares. The fair value of shares purchased under the Purchase Plan is estimated using the Black-Scholes option valuation model and the graded-vesting method with the following weighted-average assumptions for the year ended December 31, 2007 and December 31, 2006, respectively: risk-free interest rate of 3.7% and 5.1%; volatility factor of 74.4% and 78.2%; and an expected life of 1.5 years. During the year ended December 31, 2007 and December 31, 2006, the compensation cost in connection with the Purchase Plan was \$43,000 and \$24,000, respectively. During the year ended December 31, 2007 and December 31, 2006, 62,825 and 67,663 shares were issued under the Purchase Plan. As of December 31, 2007 and December 31, 2006, 543,134 and 605,959 shares were reserved for issuance under the Purchase Plan. As of December 31, 2007, the unrecorded deferred stock-based compensation balance related to the employee stock purchase plan was \$41,000 and will be recognized over an estimated weighted average amortization period of 1.5 years.

### **10. Legal Proceedings**

From time to time, the Company may be subject to legal proceedings and claims in the ordinary course of business, including claims of alleged infringement of trademarks and other intellectual property rights. The Company currently is not aware of any other legal proceedings or claims that it believes will have, individually or in the aggregate, a material adverse effect on its business, prospects, financial condition and operating results.

### **11. Related Party**

In May 2000, the Company issued loans to the Company’s President, Chief Executive Officer and Chairman of the Board, related to his exercise of 126,667 shares of options to acquire common stock. The loans were full recourse and had an interest rate of 7% per annum. In January 2006, these notes, which had a balance of \$168,000 at December 31, 2005, were repaid in full.

The Company had \$35,000 of short-term unsecured notes payable to related parties as of December 31, 2006. In 2003, the Company issued a series of short-term unsecured notes payable to members of the Board of Directors, senior management and other employees of the Company for cash. These notes bore interest at a rate of two percent (2%) per annum. In February 2007, these notes were repaid in full.

The Company had \$231,000 of short-term secured notes payable to related parties as of December 31, 2006. In 2003, the Company issued short-term senior secured notes payable to an officer who is also a member of the Board of Directors and to an affiliate of a member of senior management for cash. (Also described in Note 5) The note was secured by a lien on substantially all of the assets of the Company, including the Company’s intellectual property, other than certain equipment secured by the lessor of such equipment. In February 2007, these notes were repaid in full.

### **12. Subsequent Event**

In February 2008, the Company’s wholly-owned subsidiary, Azithromycin Royalty Sub, LLC, issued \$60.0 million in aggregate principal amount of non-convertible, non-recourse promissory notes due in 2019. The notes are secured by, and will be repaid from, royalties to be paid to us by Inspire Pharmaceuticals from sales of AzaSite in the United States and Canada. The annual cash coupon rate on the notes is 16% with interest payable quarterly in arrears beginning May 15, 2008. Net proceeds from the financing were approximately \$50.0 million after transaction costs and \$5.0 million of interest reserves.



When the AzaSite royalties received for any quarter exceed the interest payments and certain expenses due that quarter, the excess will be applied to the repayment of principal of the notes until the notes have been paid in full. The notes may be redeemed at our option, subject to the payment of a redemption premium through May 2012.

### 13. Quarterly Results (Unaudited)

The following table is a summary of the quarterly results of operations for the years ended December 31, 2007 and December 31, 2006. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

(In thousands, except per share amounts)	2007			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	\$ 929	\$ 6,617	\$ 8,271	\$ 7,944
Cost of revenues	3	260	450	269
Income (loss) from operations	(2,475)	2,163	3,577	2,370
Net income/(loss)	(2,575)	2,159	3,575	2,376
- basic	\$ (0.03)	\$ 0.02	\$ 0.04	\$ 0.03
- diluted	\$ (0.03)	\$ 0.02	\$ 0.04	\$ 0.02

(In thousands, except per share amounts)	2006			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	\$ 1	\$ -	\$ 1	\$ -
Cost of revenues	3	3	20	2
Income (loss) from operations	(4,811)	(4,570)	(3,061)	(2,626)
Net income/(loss)	(5,321)	(5,139)	(3,337)	(2,824)
- basic	(0.06)	(0.06)	(0.04)	(0.03)
- diluted	\$ (0.06)	\$ (0.06)	\$ (0.04)	\$ (0.03)

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

None

### Item 9A. Controls and Procedures

**Evaluation of Disclosure Controls and Procedures.** Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of the end of the period covered by this report (the "Evaluation Date"). Based upon the evaluation, our principal executive officer and principal financial officer concluded as of the Evaluation Date that our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act (i) is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms, and (ii) is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Disclosure controls are controls and procedures designed to reasonably ensure that information required to be disclosed in our reports filed under the Exchange Act, such as this report, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls include controls and procedures designed to reasonably ensure that such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure. Our quarterly evaluation of disclosure controls includes an evaluation of some components of our internal control over financial reporting, and internal control over financial reporting is also separately evaluated on an annual basis for purposes of providing the management report which is set forth below.



**Report of Management on Internal Control Over Financial Reporting.** Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. 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.

There are inherent limitations in the effectiveness of any system of internal control, including the possibility of human error and the circumvention or overriding of controls. Accordingly, even effective internal controls can provide only reasonable assurances with respect to financial statement preparation. Further, because of changes in conditions, the effectiveness of internal control may vary over time.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2007. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations (COSO) of the Treadway Commission in Internal Control — Integrated Framework. Based on its assessment using those criteria, our management concluded that, as of December 31, 2007, our internal control over financial reporting is effective.

The effectiveness of our internal control over financial reporting as of December 31, 2007 has been audited by Burr, Pilger & Mayer LLP, an independent registered public accounting firm, as stated in their report appearing below.

**Inherent Limitations of Disclosure Controls and Procedures and Internal Control over Financial Reporting.** It should be noted that any system of controls, however well designed and operated, can provide only reasonable, and not absolute, assurance that the objectives of the system will be met. In addition, the design of any control system is based in part upon certain assumptions about the likelihood of future events.

**Changes in Internal Control over Financial Reporting.** There were no changes in our internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f)) during the quarter ended December 31, 2007 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**Independent Registered Public Accounting Firm's Attestation Report.**

#### **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Stockholders of InSite Vision Incorporated

We have audited the internal control over financial reporting of InSite Vision Incorporated and its subsidiaries (the "Company") as of December 31, 2007, 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 maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Report of Management on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the effectiveness of the Company's internal control over financial reporting based on our audit.

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

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

regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

In our opinion, InSite Vision Incorporated and its subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2007, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of InSite Vision Incorporated and its subsidiaries as of December 31, 2007 and 2006, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2007 and our report dated March 17, 2008 expressed an unqualified opinion on those consolidated financial statements.

/s/ Burr, Pilger & Mayer LLP

Palo Alto, California

March 17, 2008

#### **Item 9B. Other Information**

Not applicable.

### **PART III**

#### **Item 10. Directors, Executive Officers and Corporate Governance**

(a) Certain information required by this Item is contained under the heading "Executive Officers of the Company" in Part I of this Annual Report on Form 10-K.

(b) Other information required by this Item will appear under the headings labeled "Nominees for Directors," "Board Committees and Meetings," "Audit Committee Matters," "Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" of our Proxy Statement in connection with the 2008 Annual Meeting of Stockholders are incorporated herein by reference.

#### **Item 11. Executive Compensation**

The information required by this Item will appear under the headings labeled "Director Compensation for 2007," "Compensation, Discussion and Analysis," "Compensation of Named Executive Officers," "Summary Compensation Table for 2007," "Grants of Plan Based Awards in 2007," "Outstanding Equity Awards at Fiscal 2007 Year End," "Option Exercises and Stock Vested in 2007," "Non-Qualified Deferred Compensation for 2007," "Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report" of our Proxy Statement and are incorporated herein by reference.

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

The information required by this Item will appear under the headings labeled “Equity Compensation Plans” and “Beneficial Ownership of Principal Stockholders, Directors and Management” of our Proxy Statement and are incorporated herein by reference.

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

The information required by this Item will appear under the headings labeled “Certain Relationships and Related Persons Transactions” and “Director Independence” of our Proxy Statement and are incorporated herein by reference.

## **Item 14. Principal Accountant Fees and Services**

### **Audit Fees**

The information required by this Item will appear under the headings labeled “Audit Committee Matters” and “Principal Accountant Fees and Services” of our Proxy Statement and are incorporated herein by reference.

## **PART IV**

## **Item 15. Exhibits and Financial Statement Schedules**

### (a)(1) Financial Statements

The Financial Statements and Report of Independent Auditors are included in a separate section of this Annual Report on Form 10-K. See index to consolidated financial statements at Item 8 of this Annual Report on Form 10-K.

### (2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable or are not required or the required information to be set forth therein is included in the Financial Statements or notes thereto included in a separate section of this Annual Report on Form 10-K. See index to consolidated financial statements at Item 8 of this Annual Report on Form 10-K.

### (3) Exhibits

See Exhibit Index on page 65 of this Annual Report on Form 10-K.

## SIGNATURES

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

Dated: March 17, 2008

### INSITE VISION INCORPORATED

By: /s/ Louis C. Drapeau

Louis C. Drapeau  
Chief Financial Officer  
(Principal Financial Officer)

## POWER OF ATTORNEY

KNOW ALL PEOPLE BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of S. Kumar Chandrasekaran and Louis C. Drapeau, his or her attorneys in fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys in fact, or his or her substitutes, may do or cause to be done by virtue thereof.

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.

<u>Name</u>	<u>Capacity</u>	<u>Date</u>
<u>/s/ S. Kumar Chandrasekaran, Ph.D.</u> S. Kumar Chandrasekaran, Ph.D.	Chairman of the Board, President, and Chief Executive Officer (Principal Executive Officer)	March 17, 2008
<u>/s/ Louis C. Drapeau</u> Louis C. Drapeau	Chief Financial Officer (Principal Financial Officer)	March 17, 2008
<u>/s/ Francis Wen-Hou Chen</u> Francis Wen-Hou Chen	Director	March 17, 2008
<u>/s/ Mitchell H. Friedlaender, M.D.</u> Mitchell H. Friedlaender, M. D.	Director	March 17, 2008
<u>/s/ John L. Mattana</u> John L. Mattana	Director	March 17, 2008
<u>/s/ Jon S. Saxe</u> Jon S. Saxe	Director	March 17, 2008
<u>/s/ Anders P. Wiklund</u> Anders P. Wiklund	Director	March 17, 2008

## EXHIBIT INDEX

<u>Number</u>	<u>Exhibit Table</u>
3.1 <sup>1</sup>	Restated Certificate of Incorporation, as amended on October 23, 2006.
3.2 <sup>2</sup>	Certificate of Designations, Preferences and Rights of Series A Convertible Preferred Stock as filed with the Delaware Secretary of State on September 11, 1997.
3.3 <sup>2</sup>	Certificate of Correction of the Certificate of Designations, Preferences and Rights of Series A Convertible Preferred Stock as filed with the Delaware Secretary of State on September 26, 1997.
3.4 <sup>3</sup>	Certificate of Designations, Preferences and Rights of Series A-1 Preferred Stock as filed with the Delaware Secretary of State on July 3, 2002.
3.5 <sup>4</sup>	Amended Bylaws.
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3 and 3.4.
10.1 <sup>5</sup>	InSite Vision Incorporated Amended and Restated Employee Stock Purchase Plan adopted October 15, 2007.
10.2 <sup>6HH</sup>	InSite Vision Incorporated 1994 Stock Option Plan (Amended and Restated as of June 8, 1998).
10.3 <sup>5HH</sup>	InSite Vision Incorporated 2007 Performance Incentive Plan.
10.4 <sup>5</sup>	Form of Nonqualified Stock Option Agreement (2007).
10.5 <sup>5</sup>	Form of Incentive Stock Option Agreement (2007).
10.6 <sup>7</sup>	Form of Indemnification Agreement between the Company and its directors and officers.
10.7 <sup>8</sup>	Form of Employee's Proprietary Information and Inventions Agreement.
10.8 <sup>9H</sup>	License Agreement dated as of October 9, 1991 by and between the Company and CIBA Vision Corporation, as amended October 9, 1991.
10.9 <sup>10</sup>	Facilities Lease, dated September 1, 1996, between the Registrant and Alameda Real Estate Investments.
10.10 <sup>11H</sup>	Timolol Development Agreement dated July 18, 1996 by and between the Company and Bausch & Lomb Pharmaceuticals, Inc.
10.11 <sup>2H</sup>	License Agreement, dated July 1, 1997, by and between the University of Connecticut Health Center and the Company.
10.12 <sup>2H</sup>	License Agreement, dated August 19, 1997, by and between the University of Rochester and the Company.
10.13 <sup>12</sup>	Amendment No. 1 to Marina Village Office Tech Lease, dated July 20, 2001 and effective January 1, 2002.
10.14 <sup>13H</sup>	License Agreement, dated December 21, 2001 by and between the Company and The University of Connecticut Health Center.
10.15 <sup>14H</sup>	ISV-403 Asset Purchase Agreement, dated December 19, 2003, between the Company and Bausch & Lomb, Inc.

10.16 <sup>15</sup>	Form of Class A Warrants issued under Subscription Agreement dated March 26, 2004.
10.17 <sup>15</sup>	Form of Class B Warrants issued under Subscription Agreement dated March 26, 2004.
10.18 <sup>15</sup>	Form of Placement Warrant issued pursuant to Placement Agreement dated February 12, 2004.
10.19 <sup>16</sup>	Form of Common Stock Warrant issued under Subscription Agreement dated May 26, 2005.
10.20 <sup>16</sup>	Form of Placement Agent Warrant, dated as of May 9, 2005.

<b>Number</b>	<b>Exhibit Table</b>
10.21 <sup>17</sup>	Warrant, dated as of October 10, 2005, for the purchase of 922,800 shares of Common Stock of the Company.
10.22 <sup>18</sup>	Form of Warrant, dated as of January 11, 2006.
10.23 <sup>18</sup>	Form of Placement Agent Warrant, dated as of January 11, 2006.
10.24 <sup>19</sup>	Form of Warrant, dated as of August 15, 2006.
10.25 <sup>20</sup>	Amendment No. 3 to Marina Village Office Tech Lease, dated November 28, 2006.
10.26 <sup>21H</sup>	Exclusive License Agreement, dated as of February 15, 2007, by and between the Company and Pfizer, Inc. and Pfizer Products, Inc.
10.27 <sup>21H</sup>	License Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.28 <sup>21H</sup>	Trademark License Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.29 <sup>21H</sup>	Supply Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.30 <sup>21HH</sup>	Change in Control Agreement for S. Kumar Chandrasekaran adopted by InSite Vision Incorporated on May 2, 2007.
23.1	Consent of Burr, Pilger & Mayer LLP, Independent Registered Public Accounting Firm.
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1	Certification of Chief Executive Officer and 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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1. Incorporated by reference to exhibits in the Company's Annual Report on Form 10-K for the year ended December 31, 1993 and the Company's Annual Report on Form 10-K for the year ended December 31, 2006.
  2. Incorporated by reference to exhibits in the Company's Registration Statement on Form S-3 (Registration No. 333-36673) as filed with the Securities and Exchange Commission on September 29, 1997.
  3. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2002.
  4. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2006.
  5. Incorporated by reference to an exhibit in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on October 19, 2007.
  6. Incorporated by reference to exhibits to the Company's Registration Statement on Form S-8 (Registration No. 333-60057) as filed with the Securities and Exchange Commission on July 28, 1998.



7. Incorporated by reference to an exhibit in the Company's Registration Statement on Form S-1 (Registration No. 33-68024) as filed with the Securities and Exchange Commission on August 27, 1993.
  8. Incorporated by reference to an exhibit in the Company's Annual Report on Form 10-K for the year ended December 31, 1993.
  9. Incorporated by reference to an exhibit to Amendment No. 1 the Company's Registration Statement on Form S-1 (Registration No. 33-68024) as filed with the Securities and Exchange Commission on September 16, 1993.
  10. Incorporated by reference to an exhibit to the Company's Annual Report on Form 10-K for the year ended December 31, 1996.
  11. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 1996.
  12. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001.
  13. Incorporated by reference to an exhibit to the Company's Annual Report of Form 10-K for the year ended December 31, 2001.
  14. Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on January 14, 2004.
  15. Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 29, 2004.
  16. Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on June 23, 2005 (File Number 333-126084).
  17. Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on October 11, 2005 (File Number 001-14207).
  18. Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on February 10, 2006 (File Number 333-131774).
  19. Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on October 13, 2006 (File Number 333-137994).
  20. Incorporated by reference to an exhibit to the Company's Annual Report of Form 10-K for the year ended December 31, 2006.
  21. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2007.
- H Confidential treatment has been granted with respect to certain portions of this agreement.
- HH Management contract or compensatory plan.

**Consent of Burr, Pilger & Mayer LLP, Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the Registration Statements on Forms S-3 (No. 333-38266, No. 333-54912, No. 333-116973, No. 333-126084, No. 333-130248, No. 333-131744 and No. 333-137994) and the Registration Statements on Forms S-8 (No. 33-75268, No. 33-80662, No. 33-93394, No. 333-29801, No. 333-60057, No. 333-79789, No. 333-43504, No. 333-72098, No. 333-117193, No. 333-126083, No. 333-133010 and No. 333-143016) of InSite Vision Incorporated of our reports dated March 17, 2008, with respect to the consolidated financial statements and the effectiveness of internal control over financial reporting which appear in this Form 10-K.

/s/ Burr, Pilger & Mayer LLP

Palo Alto, California

March 17, 2008

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**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER  
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, S. Kumar Chandrasekaran, Ph.D., certify that:

1. I have reviewed this annual report on Form 10-K of InSite Vision Incorporated;
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)) for the registrant 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 controls over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 17, 2008

/s/ S. Kumar Chandrasekaran, Ph.D.

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S. Kumar Chandrasekaran, Ph.D.  
Chief Executive Officer  
(Principal Executive Officer)



**CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER  
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Louis C. Drapeau, certify that:

1. I have reviewed this annual report on Form 10-K of InSite Vision Incorporated;
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)) for the registrant 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 controls over financial reporting, to the registrant's auditors and the audit committee of 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 reasonable likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 17, 2008

/s/ Louis C. Drapeau

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Louis C. Drapeau  
Chief Financial Officer  
(Principal Financial Officer)

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

I, S. Kumar Chandrasekaran, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of InSite Vision Incorporated on Form 10-K for the annual period ended December 31, 2007 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report of InSite Vision Incorporated on Form 10-K fairly presents, in all material respects, the financial condition and results of operations of InSite Vision Incorporated.

By: /s/ S. Kumar Chandrasekaran, Ph.D.

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Name: S. Kumar Chandrasekaran, Ph.D.

Title: Chief Executive Officer (Principal Executive Officer)

Date: March 17, 2008

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

I, Louis C. Drapeau, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of InSite Vision Incorporated on Form 10-K for the annual period ended December 31, 2007 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report of InSite Vision Incorporated on Form 10-K fairly presents, in all material respects, the financial condition and results of operations of InSite Vision Incorporated.

By: /s/Louis C.Drapeau

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Name: Louis C. Drapeau

Title: Chief Financial Officer (Principal Financial Officer)

Date: March 17, 2008

The signed originals of these two written statements required by Section 906 have been provided to the Registrant and will be retained by the Registrant and furnished to the Securities and Exchange Commission or its staff upon request.

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