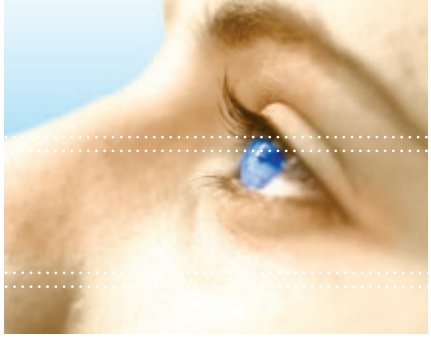
FOCUSED

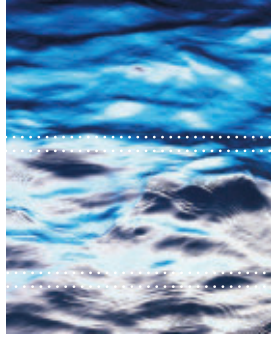
on Shareholder Value

2008 ANNUAL REPORT

InSiteVision

Solutions for Sight



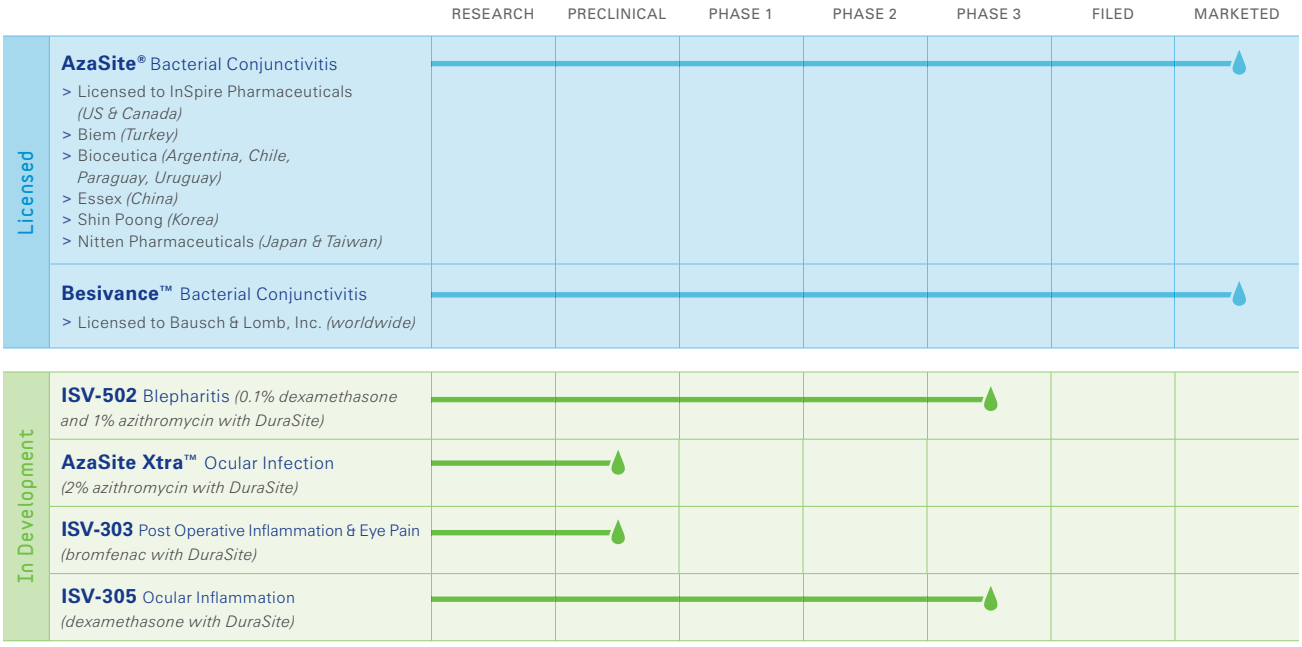


ABOUT INSITE VISION

INSITE VISION DEVELOPS NEW AND SUPERIOR OPHTHALMIC PRODUCTS FOR UNMET EYE CARE NEEDS.

Our company is recognized for the discovery and development of novel ocular pharmaceutical products based on its DuraSite® bioadhesive polymer core technology, an innovative platform that extends the duration of drug delivery on the eye's surface, thereby reducing frequency of treatment and improving the efficacy of topically-delivered drugs. The DuraSite platform is currently employed in two commercial products for the treatment of bacterial eye infections, AzaSite® (azithromycin ophthalmic solution) 1% and Besivance™ (besifloxacin ophthalmic suspension) 0.6%. AzaSite is approved in the United States and Canada and currently marketed in the United States by InSite Vision's commercial partner, Inspire Pharmaceuticals. Besivance was approved by the U.S. Food and Drug Administration in the second quarter 2009 and is currently being marketed by Bausch & Lomb and Pfizer Inc. in the United States. InSite Vision has also formed multiple strategic licensing and distribution agreements with qualified partners to market AzaSite in select countries in Asia and South America upon regulatory approval in those regions. InSite Vision's ophthalmic product development pipeline includes ISV-502 and additional product candidates leveraging the company's core technologies.

PRODUCT PIPELINE



October 28, 2009

DEAR SHAREHOLDERS

It has been a productive year for InSite Vision.

Last fall, with a new Board of Directors in place, we initiated a comprehensive evaluation of our business, analyzing our products, pipeline, expertise, market conditions / opportunities, and financial position. Our goal was to develop a well-considered strategy to capitalize on InSite Vision's core assets and build value for our shareholders, while pursuing our mission of advancing novel ophthalmic products to benefit patients.

As a result of this process, we identified the following strategic priorities:

- Support and extend sales of AzaSite® (azithromycin ophthalmic solution) 1% in the United States and abroad;
- Position existing pipeline and platform assets for potential partnering or future development;
- Explore strategic transactions (including in-licensing and M&A opportunities) that would complement our strengths and foster R&D growth; and
- Conserve our cash resources.

We are consistently executing against this plan and have a number of positive achievements to report.

Supporting AzaSite Sales

We continue to work closely with our commercial partner, Inspire Pharmaceuticals, to support their efforts to increase AzaSite sales in the United States. During the first three quarters of 2009, prescriptions of AzaSite have risen 92% over the same period of 2008.

Beyond the increase in AzaSite sales, we believe there is significant opportunity for further growth in existing and new markets. Earlier this year, Inspire Pharmaceuticals initiated two Phase 2 clinical trials intended to evaluate the efficacy and safety of AzaSite in the treatment of blepharitis, a common condition characterized by chronic inflammation of the eyelid. Inspire has announced that it expects results from both Phase 2 trials in the first half 2010. We are entitled to a 25% royalty from Inspire for North American net sales of AzaSite.

Extending AzaSite's availability internationally has also been a key priority. In March, we received regulatory approval of AzaSite from the Therapeutic Products Directorate of Health Canada for the treatment of bacterial conjunctivitis. Inspire Pharmaceuticals is also our commercial partner in Canada.

In addition, we signed an international licensing and distribution agreement in March with Nitten Pharmaceuticals to commercialize AzaSite in Japan and Taiwan. And while economic conditions have delayed entering into a commercial partnership in Europe, we remain in active negotiations with several potential European commercial partners. These international agreements are in addition to those we have forged with commercial partners for AzaSite in South Korea, four countries in South America, Turkey and China. In all of these countries, our partners are responsible for obtaining regulatory approvals and commercializing AzaSite after approval. Internationally, we will receive low double-digit royalties from our partners for AzaSite sales.

Maximizing the Value of Our Core Pipeline and Platform Assets

Our proprietary DuraSite® drug delivery platform remains a valuable core asset for our company. DuraSite is designed to enhance the retention time of therapeutic agents on the surface of the eye — thereby achieving higher concentrations of drug and less frequent dosing.

In addition to AzaSite, DuraSite has been licensed and applied successfully to Bausch & Lomb's Besivance™ (besifloxacin ophthalmic suspension) 0.6% for the treatment of bacterial conjunctivitis. Earlier this year, Bausch & Lomb received approval from the U.S. Food

October 28, 2009

DEAR SHAREHOLDERS

and Drug Administration (FDA) for Besivance which is being marketed in the U.S. by Bausch & Lomb and their co-promotion partner, Pfizer Inc. We receive a mid-single digit royalty from Bausch & Lomb on global net sales of Besivance.

Cultivation of new partnerships that leverage our existing technology platform, product, pipeline and intellectual assets will drive value for InSite.

DuraSite has also been utilized in the formulation of multiple product concepts, including ISV-502, our late-stage clinical product combining a topical antibiotic and a corticosteroid to treat infection and inflammation of the eyelid and conjunctiva.

We have worked this year to clarify the best regulatory path forward for ISV-502. In December 2008, we reported data from our Phase 3 clinical trial of ISV-502. These data were positive, but did not meet the FDA's requirement for combination drugs to be superior to each drug used separately. In April, we met with the FDA to review data from the Phase 3 trial. Following an encouraging meeting with the FDA, we have a clear move-forward plan for the development of ISV-502 for the treatment of blepharitis — a potentially broader indication than originally planned. As a next step in product development, we will seek a commercial partner with whom to conduct a pilot clinical study in this indication.

We have also generated earlier-stage product candidates combining DuraSite with non-steroidal anti-inflammatory agents for use in treating postsurgical ocular inflammation. We are seeking licensing partners for some of our early-stage product candidates, and hope to work with new partners on the development of novel applications of our DuraSite technology.

Evaluating Our Strategic Opportunities

In line with a continued exploration of partnering opportunities for our core assets, we have also sought to explore partnerships that could take advantage of InSite's strengths and fuel future growth. As part of our assessment of the company and its strategy, InSite's leadership team developed detailed criteria for screening new products and/or technology licensing or M&A opportunities. We engaged Piper Jaffray & Co. to help us identify potential prospects. We look forward to updating investors as suitable opportunities solidify.

Executing on Plan with Operational Discipline

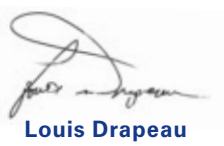
Our strategy this past year has included conserving our financial resources while taking advantage of strategic opportunities that we believe will increase shareholder value. Implementation of our business objectives is guided by our belief that a disciplined combination of executing on plan and conserving our cash will provide us with greater operating flexibility. For the nine months ended September 30, 2009, our cash burn of $10.7 million was down 63% from the same period a year ago.

InSite Vision possesses strong fundamentals — including a solid cash position, commercial products, a portfolio of pipeline programs, an innovative platform technology and a veteran leadership team. This combination of strong fundamentals and clear strategic objectives is designed to drive future growth.

I look forward to keeping you updated on our continued progress through what promises to be a transformational time for InSite Vision.

Thank you for your support.

Sincerely,



Louis Drapeau
Interim Chief Executive Officer and
Vice President, Chief Financial Officer

FORM 10-K

2008

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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, 2008

OR

☐ **Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
Commission file number: 1-14207

INSITE VISION INCORPORATED
(Exact name of registrant as specified in its charter)

Delaware	**94-3015807**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

965 Atlantic Avenue, Alameda CA 94501
(Address of principal executive offices) (Zip Code)

(510)-865-8800
(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.01 par value per share	New York Stock Exchange Alternext US

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

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 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 (§ 229.405) 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 ☒

The aggregate market value of registrant's Common Stock, $0.01 par value, held by non-affiliates of the Registrant as of June 30, 2008 was approximately $36,277,543 (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 10, 2009: 94,681,618.

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 definitive proxy statement (the "Proxy Statement") to be mailed to stockholders in connection with the solicitation of proxies for the Registrant's 2009 annual meeting of stockholders (the "Annual Meeting") are incorporated herein by reference in Parts II and III of this Annual Report on Form 10-K to the extent stated herein.

ANNUAL REPORT ON FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2008

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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

THE COMPANY

Item 1. Business

InSite Vision Incorporated ("InSite" or the "Company") is an ophthalmic product development company committed to advancing ophthalmic pharmaceutical products to address unmet eye care needs. Our current portfolio of ophthalmic pharmaceutical products is based on our proprietary DuraSite ® drug delivery technology.

Our DuraSite sustained drug 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, development and commercial support efforts on the following topical anti-infective products that formulate the antibiotic azithromycin with our DuraSite drug delivery technology.

- AzaSite ® (azithromycin ophthalmic solution) 1% is a DuraSite formulation of azithromycin developed as a broad spectrum ocular antibiotic and approved by the U.S. Food and Drug Administration (FDA) in April 2007 to treat bacterial conjunctivitis (pink eye). AzaSite was launched by Inspire Pharmaceuticals in August 2007. The key advantages of AzaSite are a significantly reduced dosing regimen leading to better compliance and patient outcome and a lowered probability of bacterial resistance based on high tissue concentration.
- ISV-502 is a DuraSite formulation of azithromycin and dexamethasone in development for the treatment of ocular inflammation and infection (blepharitis and/or blepharoconjunctivitis) for which there is no FDA-approved treatment. We completed the first of two pivotal Phase 3 trials in November 2008.
- ISV-405, is a DuraSite formulation utilizing a higher percentage of azithromycin, and is in preclinical development for the treatment of ocular infection for markets outside the United States.

Business Strategy.

Our business strategy includes three key pillars:

1. **Support and extend sales of AzaSite.** Working with our North American commercial partner, Inspire Pharmaceuticals, we will seek to increase AzaSite sales through a variety of approaches, including the evaluation of AzaSite for additional indications such as blepharitis, or inflammation of the eyelid. We are also seeking additional commercial partners outside the United States to market AzaSite in Japan and Europe.

2. **Develop and monetize our pipeline of ocular product candidates.** We plan to conduct preclinical and clinical testing of product candidates in our portfolio, and then partner with pharmaceutical companies to complete clinical development, manufacture, and market these products.

3. **Invest in long-term Research and Development opportunities.** We will seek to in-license or acquire promising product candidates and technologies from companies and academic institutions, then apply our expertise to create novel differentiated ophthalmic product opportunities. We may also utilize our DuraSite technology platform for the formulation of new ocular product candidates using either non-proprietary drugs or compounds originally developed by others for non-ophthalmic indications.

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.

Ophthalmic Anti-Infective Market

Today, eye infections are routinely treated with topical antibiotics as well as antibiotic/corticosteroid combination products. The ocular anti-infective market represented global sales of $1.8 billion in 2008 according to Hygea Strategies LLC IMS-based data and comprises two separate product segments:

- Ocular antibiotic products
- Ocular antibiotic/corticosteroid combination products

We have concentrated most recently on the need for differentiated topical anti-infectives. We continue to support the need for differentiated topical products to treat eye and eye-lid infections. Some of these infections are either under-treated or do not have an FDA-approved product 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 have been utilized by eye care physicians:

- *Eye Infections.*
  - *Acute bacterial conjunctivitis* (pink eye) is a common condition experienced by most people at some point in their lives, but is especially prevalent among children. 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. As it is a contagious condition, immediate treatment is recommended. Our ocular antibiotic, AzaSite, is targeted at treating this 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 a 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, ISV-502, is targeted at this unmet need by treating both the infection and inflammation.

AzaSite Products and Product Candidates

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

Principal AzaSite Products and Product Candidates
Active Programs

Product	Indications	Anticipated Benefits	Status
Topical Anti-infectives			
AzaSite	Bacterial conjunctivitis (pink eye)	Broad spectrum antibiotic with reduced dosing frequency	*Approved and launched in US *New Drug Submission (NDS) filed in Canada
ISV-502	Blepharitis/ Blepharoconjunctivitis	Broad spectrum antibiotic combined with an anti-inflammatory corticosteroid with reduced dosing frequency to treat both inflammation and infection	*Pivotal Phase 3(a) trial completed
ISV-405	Eye infections	Broad spectrum antibiotic with reduced dosing frequency	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 seven-day dosing period using our proprietary DuraSite technology. The eye drop is designed to enable superior bactericidal activity against common ocular pathogens and even difficult bacteria such as 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. Clinical studies have shown that AzaSite is well tolerated and efficacious.

In August 2007, Inspire Pharmaceuticals commercially launched AzaSite (azithromycin ophthalmic solution) 1% in the United States pursuant to their license of AzaSite from InSite and approval by the FDA in April 2007.

In the United States, our commercial partner Inspire focuses on ophthalmologists, optometrists, pediatricians, and primary care physicians who routinely treat eye infections. AzaSite is positioned to compete favorably with the newer fourth 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.

ISV-502 in Phase 3 Trials for Blepharitis*/ Blepharoconjunctivitis*

Expansion of our AzaSite product into a larger franchise is the development of a combination of azithromycin with platform corticosteroid (dexamethasone) for the treatment of blepharitis/ 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 (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 ISV-502 was well tolerated and 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 ISV-502 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 for ISV-502. 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 first Phase 3(a) trial, which included lid margin redness, lid swelling, conjunctival redness, ocular discharge, and lid irritation in at least one eye.

The Phase 3(a) trials tested a total of 417 patients. The dosing regimen consists of one drop in the eye and one on the eyelid, two times a day for 14 days. The trial design included three treatment arms with the objective of demonstrating the superiority of ISV-502 in treating blepharoconjunctivitis over AzaSite and dexamethasone.

Preliminary results from the Phase 3(a) trial indicate that ISV-502 improved clinical outcomes as compared to treatment with AzaSite alone or dexamethasone alone in bacterial eradication and the reduction of inflammatory signs and symptoms, respectively. However, an initial evaluation of the data indicates that the trial did not achieve its primary endpoint as defined by the protocol. In addition, ISV-502 was very well tolerated.

We plan to discuss results from this trial with the FDA and, based on this meeting, we will determine our plans for a confirmatory Phase 3 clinical trial or additional testing of the compound. We currently plan to seek a partner for ISV-502 to work with on the final stages of product development and commercialization.

ISV-405: Pre-clinical Development for Ocular Infections in International Markets

We are in the early stages of developing *ISV-405* , a product candidate with a higher percentage of azithromycin (2%) as part of its formulation than with AzaSite (1%). ISV-405 is being developed for the treatment of eye infections. We intend to partner this product for markets outside of the United States.

DuraSite Sustained Delivery Technology

At the core of our AzaSite franchise is our proprietary DuraSite drug delivery technology. Our DuraSite sustained drug 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 and proven drug products results in differentiated products that have increased efficacy and improved compliance through a 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. In addition to its formulation with azithromycin in our AzaSite family of products, our DuraSite technology may be used in the formulation of new ocular product candidates using either non-proprietary drugs or compounds developed by others for non-ophthalmic indications.

Physical Properties. DuraSite is composed of a cross-linked polyacrylic acid polymer, water and salts. We have developed considerable knowledge of 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 $3x10^7$ 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. It will also be utilized in Bausch & Lomb's new anti-infective eye drop besifloxacin ophthalmic suspension, 0.6%, which the FDA Dermatologic and Ophthalmic Drugs Advisory Committee recently recommended approval. Bausch & Lomb's intent is to bring this product to market in the first half of 2009.

Additional Research and Development Opportunities

In addition to products leveraging our DuraSite technology, we will seek to in-license or acquire promising product candidates and technologies from academic institutions and other companies and to apply our expertise to create novel differentiated ophthalmic product opportunities.

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 key agreements.

Shin Poong Pharm Co., Ltd. In December 2007, we entered into an international licensing and distribution agreement for AzaSite with Shin Poong, Seoul, South Korea, one of the top ten South Korean pharmaceutical companies. This was the first international agreement for AzaSite outside of North America. Under the terms of the agreement, the Company granted exclusive rights to Shin Poong to commercialize AzaSite for ocular bacterial infection in South Korea.

Bioceutica S.A. In March 2008, the Company entered into a licensing and distribution agreement for AzaSite with Bioceutica S.A. in Argentina. Under the terms of the agreement, the Company granted exclusive rights to Bioceutica to commercialize AzaSite for ocular bacterial infection in Argentina, Chile, Paraguay and Uruguay.

Biem Pharmaceuticals. In April 2008, the Company entered into a licensing and distribution agreement for AzaSite with Biem Pharmaceuticals in Turkey. Under the terms of the agreement, the Company granted exclusive rights to Biem Pharmaceuticals to commercialize AzaSite for ocular bacterial infection in Turkey.

Essex Bio-Technology. In May 2008, the Company entered into a licensing and distribution agreement for AzaSite with Essex Bio-Technology in the People's Republic of China. Under the terms of the agreement, the Company granted exclusive rights to Essex Bio-Technology to commercialize AzaSite for ocular bacterial infection in the People's Republic of China.

In all of these agreements, the licensee is responsible for obtaining regulatory approval and will generally pay the Company a double digit royalty on net sales of AzaSite in these countries, if approved by regulatory authorities. The Company will be responsible for providing AzaSite inventory to these licensees at a fee per respective agreed upon licensing agreement.

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 ISV-502. 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 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 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 (NDA), to Inspire. We are also responsible for obtaining regulatory approval of AzaSite in Canada. On November 30, 2007, we filed a 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 the U.S. and Canada.

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 documentation 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.

In addition, 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 expires in 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. According to plan, the AzaSite NDA was transferred to Inspire 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 Co., Ltd. (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. 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, eight 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 three applications pending. At least five other patent applications by us relating to the foregoing and other aspects of our business and potential business are also pending. Foreign counterparts of our patents as well have filed/issued 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 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.

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, 2008, our research and development staff numbered 26 people, of whom 7 have Ph.D.s. Our research and development expenses for the years ended December 31, 2008, 2007 and 2006 were:

Research and Development Cost by Program
(in millions)

Program	2008	2007	2006
ISV-502	$12.0	$ 6.0	$ 2.7
AzaSite	0.6	2.7	6.1
AzaSite Otic	1.3	1.3	—
ISV-405	0.6	0.4	—
Other	1.7	—	0.1
Total	$16.2	$10.4	$ 8.9

In 2008, our ISV-502 program activities consisted primarily of the Phase 3(a) clinical trial and preparation for the production of Canadian AzaSite registration batches at our contract manufacturing site. Our activities related to our AzaSite Otic program mainly consisted of preclinical testing prior to its discontinuation in July 2008. Our ISV-405 activities also mainly related to preclinical experiments. Further development of this program has been deferred. Other program activities consisted primarily of new product development and activities related to commercializing AzaSite in the international markets.

In 2007, our ISV-502 program activities related to 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(a) clinical trial. Our AzaSite program activities included producing United States registration batches at our contract manufacturing site and assembling and filing the application for regulatory approval in Canada. Our activities related to the AzaSite Otic program mainly consisted of preclinical testing to support filing of an IND. Our ISV-405 activities mainly related to preclinical experiments.

In 2006, our ISV-502 program activities mainly focused on preclinical testing, preparation of an IND and initiation of Phase 1 clinical trials. 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.

Although the majority of our personnel were focused on our ISV-502 program in 2008, due to our limited personnel and the number of projects that we are developing, our personnel are involved in a number of projects at the same time. Accordingly, the majority of our research and development 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, ISV-502 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 in the U.S. and abroad, 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, Seoul, South Korea, one of the top ten South Korean pharmaceutical companies. Under the terms of the agreement, InSite grants exclusive rights to Shin Poong to commercialize AzaSite for ocular bacterial infection in South Korea.

Bioceutica S.A. In March 2008, the Company entered into a licensing and distribution agreement for AzaSite with Bioceutica S.A. in Argentina. Under the terms of the agreement, the Company granted exclusive rights to Bioceutica to commercialize AzaSite for ocular bacterial infection in Argentina, Chile, Paraguay and Uruguay.

Biem Pharmaceuticals. In April 2008, the Company entered into a licensing and distribution agreement for AzaSite with Biem Pharmaceuticals in Turkey. Under the terms of the agreement, the Company granted exclusive rights to Biem Pharmaceuticals to commercialize AzaSite for ocular bacterial infection in Turkey.

Essex Bio-Technology. In May 2008, the Company entered into a licensing and distribution agreement for AzaSite with Essex Bio-Technology in the People's Republic of China. Under the terms of the agreement, the Company granted exclusive rights to Essex Bio-Technology to commercialize AzaSite for ocular bacterial infection in the People's Republic of China.

In all of these agreements, the licensee is responsible for obtaining regulatory approval and will generally pay the Company a double-digit royalty on net sales of AzaSite in these countries, if approved by regulatory authorities. The Company will be responsible for providing AzaSite inventory to these licensees at a fee per respective agreed upon licensing agreement.

Inspire Pharmaceuticals, Inc. 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. We anticipate that ISV-403 will be approved in the United States in the first half of 2009.

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 is anticipated to grow and will become even more competitive going forward as the prevalence of eye disease increases, leading 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. Some of 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 at a faster rate, thereby gaining greater market acceptance than the therapies that we are developing or have developed with our more limited resources. By being first to the market, these competitors may also succeed in obtaining cost advantages or intellectual property rights that would limit our ability to develop and commercialize our own product opportunities. Consequently, they might obtain a more timely and effective regulatory approval for the commercialization of their products in comparison to our timeline.

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. While there are many other large- and medium-sized companies participating in the ophthalmic market, smaller companies such as our own find it challenging to successfully develop and market products without entering into collaborations.

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 as well as many in development by prominent competitors. Therefore, in order to penetrate these competitive mature markets, 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 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;
- 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:

Name	Position
Mark Abelson, M.D.	Associate Clinical Professor of Ophthalmology, Department of Ophthalmology, Harvard Medical School
D. Bruce Burlington, M.D.	Consultant, Regulatory
Chandler R. Dawson, M.D.	Emeritus Professor, Department of Ophthalmology, University of California, San Francisco
Syd Gilman, Ph.D.	Partner, Trident Rx Consultant Service
Allan Flach, MD, Pharm D	Director, Evening Ophthalmology Outpatient Unit, UCSF Director, Ophthalmic Clinical Pharmacology, Department of Veterans Affairs, San Francisco
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
Gholam Payman, M.D.	Associated Retina Consultants, Phoenix AZ
James G. Shook, Ph.D.	President, Jim Shook Research, Inc.
Christopher Ta, M.D.	Associate Professor of Ophthalmology, Stanford Medical Center

Executive Officers of the Company

As of March 13, 2009, our executive officers were as follows:

Name	Age	Title
Louis Drapeau	65	Interim Chief Executive Officer, Vice President and Chief Financial Officer
Lyle M. Bowman, Ph.D.	60	Vice President, Development
David F. Heniges	65	Vice President and General Manager, Commercial Opportunities
Kamran Hosseini, M.D., Ph.D.	44	Vice President, Clinical Affairs and Chief Medical Officer
Surendra Patel	54	Vice President, Operations

Louis Drapeau joined us on October 1, 2007 as Vice President and Chief Financial Officer and was appointed the interim Chief Executive Officer in October 2008. 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.

Lyle M. Bowman joined us in October 1988 as Director of Drug Delivery Systems. Previously, Dr. Bowman had worked at Syntex Ophthalmics as Manager/Director of Analytical Polymer Characterization working on contact lenses and solutions from 1979 through September 1988. From 1989 to 1991, Dr. Bowman served as Vice President, Science and Technology. From 1991 to 1995, he served as Vice President, Development, and from 1995 to 2008 served as Vice President Development and Operations. Dr. Bowman currently is Vice President Development, holds a Ph.D. in Physical Chemistry from the University of Utah and has considerable experience in material science as applied to ophthalmic products.

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 KeraVision, 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.

Kamran Hosseini joined us in February 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 the resident expert 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.

Surendra Patel joined us in April 2008 as Vice President, Operations. From 2002 to 2008, Mr. Patel served as Senior Director, Manufacturing Operations at Nektar Therapeutics where he managed clinical and commercial manufacturing operations and played a strategic role in the selection of domestic and international contract manufacturing sites. Mr. Patel has more than 30 years of development and operational experience in various management positions at pharmaceutical and biotechnology companies, including Syntex, Roche Bioscience, Oread Inc., and DrugAbuse Sciences. Mr. Patel has a Bachelor of Science degree in pharmaceutical formulation from De Montford University, Leicester, United Kingdom.

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.

Employees

As of December 31, 2008, we had 36 employees, 34 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. We must receive approval in other countries prior to marketing AzaSite in such countries. 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 a NDA. Successful development of pharmaceutical products is highly uncertain. Products that appear promising in research or development, including ISV-502, 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 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; or
- is not able to compete with superior, equivalent, more cost-effective or more effectively promoted products offered by competitors.

Therefore, our research and development activities, including ISV-502, 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 the 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 recently completed our Phase 3(a) clinical trial for our ISV-502 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 ISV-502 and any other product candidates may take over a year to complete. Furthermore, we could encounter problems that might 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.

Preliminary results from the Phase 3(a) clinical trial of ISV-502 for the treatment of blepharoconjunctivitis showed improved clinical outcomes as compared to treatment with a corticosteroid alone or antibiotic alone in the reduction of inflammatory signs and symptoms and bacterial eradication, respectively. In addition, ISV-502 was very well tolerated. However, an evaluation of the data indicated that the trial did not achieve its primary endpoint as defined by the protocol. The Company will utilize data from this Phase 3(a) trial in the finalization of a planned confirmatory Phase 3 clinical study. The Company anticipates discussing the results of this trial with the U.S. Food and Drug Administration (FDA) in the second quarter of 2009. Following these discussions, the Company will announce anticipated timing for initiating a second Phase 3 clinical trial.

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 ISV-502. 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;
- the efforts and success of our collaborators in marketing the product;
- 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 our partner 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 a 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 recent Phase 3(a) trial for ISV-502, 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 or use our products

Even if the FDA approves our product candidates, physicians and patients may not accept or 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 products;
- cost-effectiveness of our products relative to competing products;
- actual or 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 the February 2008 issuance of $60 million in aggregate principal amount of non-convertible, non-recourse promissory notes due in 2019, or the 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 whom 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 Note 5 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 in these territories, 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 primarily to eye care professionals, and to a lesser degree, pediatricians and primary care providers. However, Inspire has no prior experience calling on pediatricians and primary care physicians and has focused its sales efforts on eye care professionals. Pediatricians and primary care physicians write more than 67% of prescriptions to ophthalmic antibiotics. 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 have experienced senior management departures, which could harm our ability to attract and retain key employees.

Dr. S. Kumar Chandrasekaran, our former chief executive officer and president, concluded his employment with us in October 2008 and Louis Drapeau, our vice president and chief financial officer, was appointed to succeed him in the position of interim chief executive officer. The new Board of Directors elected September 23, 2008 has commenced a search for a new chief executive officer. While this search has been suspended until we further execute on our strategic priorities, there is no guarantee this search will be successful when, and if, recommenced. There is no guarantee that Mr. Drapeau will remain at our Company until a new chief executive officer can be recruited or for an extended period of time. We are currently highly dependent on Mr. Drapeau and the loss of Mr. Drapeau's services could significantly delay or prevent the achievement of planned development objectives. Furthermore, the changes in the composition of our Board of Directors and chief executive officer may cause us to lose additional employees and may harm the ability of our senior management team to coalesce, motivate our employees and address challenges faced by our Company. We are also highly dependent on Dr. Lyle Bowman, our vice president, development. We do not carry a life insurance policy on Mr. Drapeau or on Dr. Bowman.

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 the challenges faced by our Company 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 NDA. 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 Ocuflox 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 not material for the years ended 2008, 2007, or 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, 2008, 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, 2008. 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, 2008. 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. A group of our stockholders recently prevailed in a proxy contest that resulted in the replacement of all members of our Board of Directors.

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; we have not paid dividends in the past and do not anticipate doing so in the future

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 twelve months ended December 31, 2008, our closing stock price fluctuated from a high of $0.87 to a low of $0.18. 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.

Our common stock may be delisted from the New York Stock Exchange Alternext US

On February 26, 2009, the Company received a notice from NYSE Alternext US LLC, or the Exchange, that our common stock is subject to immediate delisting proceedings because we were not in compliance with (a) Section 1003(a)(i) of the Exchange's Company Guide, or the Company Guide, because our shareholders' equity was less than the required $2,000,000 and we had losses from continuing operations and net losses in two of our three most recent fiscal years or (b) Section 1003(a)(ii) of the Company Guide because our shareholders' equity was less than the required $4,000,000 and we had losses from continuing operations and net losses in three of our four most recent fiscal years.

The Company has requested an oral hearing to appeal the determination. There is no assurance that the decision will be overturned at this hearing. If the decision is not overturned, our common stock would be subject to delisting proceedings immediately following the hearing. Delisting would harm the trading volume and liquidity of our common stock and, as a result, the market price for our common stock might become more volatile. Delisting could also cause a reduction in the number of investors willing to hold or acquire our common stock, transactions in our common stock could be delayed, and securities analysts' and news media coverage of us may be further reduced. These factors could result in lower prices and larger spreads in the bid and ask prices for shares of common stock. Delisting could also make it more difficult for us to raise additional capital.

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. 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

The Company is subject to various claims and legal actions during the ordinary course of our business. We believe that there are currently no claims or legal actions that would have a material adverse impact on our financial position, operations or potential performance.

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

None.

PART II

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

Market Information

Since September 30, 2008, our common stock has traded on The New York Stock Exchange Alternext US under the symbol "ISV." From June 10, 1998 to September 29, 2008, our common stock was traded on The American Stock Exchange under the symbol "ISV". The New York Stock Exchange Euronext acquired the American Stock Exchange on September 30, 2008. 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 New York Stock Exchange Alternext US or The American Stock Exchange for the periods indicated. These prices do not include retail mark-ups, mark-downs or commissions.

2008	High	Low
First Quarter	0.87	0.57
Second Quarter	0.71	0.53
Third Quarter	0.66	0.43
Fourth Quarter	0.47	0.18
2007	**High**	**Low**
First Quarter	1.73	1.42
Second Quarter	1.79	1.42
Third Quarter	1.49	1.04
Fourth Quarter	1.32	0.69

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

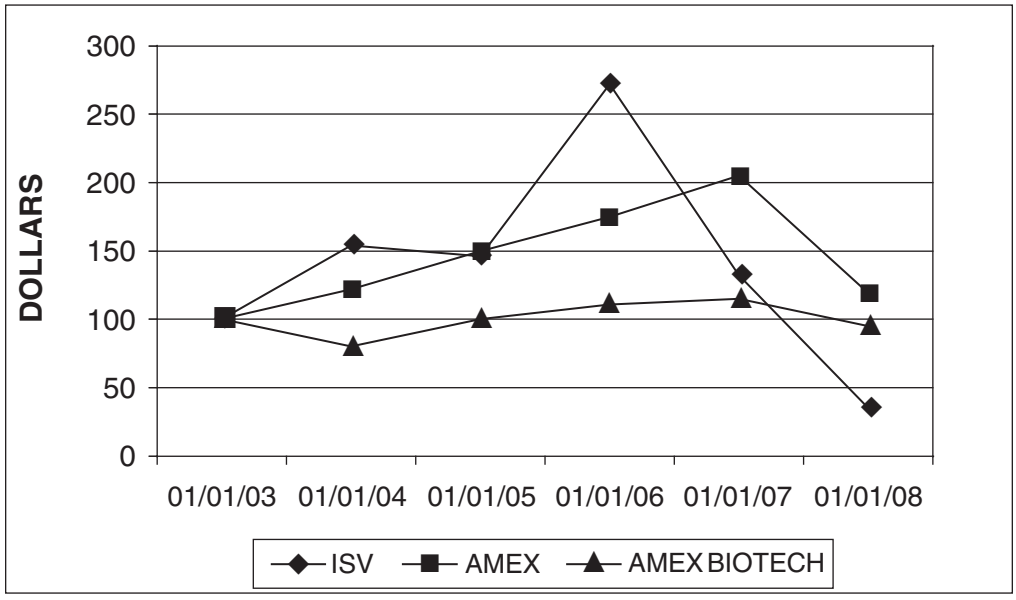
Information regarding employee stock based compensation is provided in Note 9 in the Notes to the Consolidated Financial Statements in Item 8 of Part II of this Annual Report on Form 10-K. The remaining information required by this Item will be included in our Proxy Statement and such required information is incorporated herein by reference.

As of March 10, 2009, we had approximately 205 stockholders of record of our Common Stock. On March 10, 2009, the last sale price reported on The New York Exchange Alternext US for our common stock was $0.17 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, 2003 through December 31, 2008 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, 2003 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
12/31/03	100	100	100
12/31/04	154	122	80
12/31/05	146	150	100
12/31/06	272	175	111
12/31/07	132	205	115
12/31/08	35	119	95

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 statues.

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, 2008 (in thousands except per share amounts):

	Year Ended December 31,				
(in thousands, except per share data)	2008	2007	2006	2005	2004
Consolidated Statements of Operations Data					
Revenues	$ 13,706	$ 23,761	$ 2	$ 4	$ 542
Cost of revenues	630	982	28	14	14
Operating expenses:					
Research and development	16,242	10,384	8,890	10,690	6,788
General and administrative	8,251	6,760	6,182	4,510	3,826
Severance	1,909				
Total expenses	26,402	17,144	15,072	15,200	10,614
Gain on sale of assets	—	—	—	—	4,616
Interest (expense) and other income, net	(7,984)	(100)	(1,513)	(5)	(44)
Net income (loss)	(21,310)	5,535	(16,611)	(15,215)	(5,514)
Net income (loss) per share:					
Earnings (loss) per share—basic	$ (0.23)	$ 0.06	$ (0.19)	$ (0.21)	$ (0.11)
Earnings (loss) per share—diluted	$ (0.23)	$ 0.06	$ (0.19)	$ (0.21)	$ (0.11)
Weighted average shares used in per-share calculation:					
—basic	94,607	94,168	88,339	72,647	47,984
—diluted	94,607	100,110	88,339	72,647	47,984

	As of December 31,				
(in thousands)	2008	2007	2006	2005	2004
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 37,456	$ 11,532	$ 986	$ 4,027	$ 5,351
Working capital, exclusive of deferred revenue	35,068	9,589	(6,836)	(3,424)	3,515
Total assets	44,943	15,012	2,439	5,079	5,696
Secured notes payable	60,000	—	—	—	—
Accumulated deficit	(168,837)	(147,527)	(153,062)	(136,451)	(121,236)
Total stockholders' equity (deficit)	$ (19,506)	$ 746	$ (6,302)	$ (2,545)	$ 3,601

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

We are an ophthalmic product development company committed to advancing ophthalmic pharmaceutical products to address unmet eye care needs. Our current portfolio of products is based on our proprietary DuraSite® drug delivery technology.

Our DuraSite® sustained drug 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 have focused our research and development and commercial support efforts on the following topical anti-infective products that formulate the antibiotic azithromycin with our DuraSite® drug delivery technology.

- AzaSite® (azithromycin ophthalmic solution) 1% is a DuraSite formulation of azithromycin, was developed to serve as a broad spectrum ocular antibiotic and 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.
- ISV-502 is a DuraSite formulation of azithromycin and dexamethasone is under development for the treatment of ocular inflammation and infection (blepharitis and/or blepharoconjunctivitis) for which there is no FDA approved indicated treatment; we completed the first of two pivotal Phase 3 trials in November 2008.
- ISV-405 is a DuraSite formulation with a higher percentage of azithromycin, is in preclinical development for the treatment of ocular infection for markets outside the United States.

Major Developments and Events in 2008

Our major developments and events in 2008 included:

- increased sales of AzaSite by Inspire in the United States;
- completed our Phase 3(a) trial for ISV-502;
- execution of a licensing agreement with Bioceutica in March 2008 to commercialize AzaSite for ocular bacterial infection in Argentina, Chile, Paraguay and Uruguay;
- execution of a licensing agreement with Essex Bio-Technology in May 2008 to commercialize AzaSite for ocular bacterial infection in China including the Mainland, Hong Kong and Macao;
- execution of a licensing agreement with Biem Pharmaceuticals in April 2008 to commercialize AzaSite for ocular bacterial infection in Turkey;
- the February 2008 issuance of $60 million in aggregate principal amount of secured, non-convertible, non-recourse promissory notes due in 2019 (the "AzaSite Notes");
- discontinuation of pre-clinical development of AzaSite Otic (ISV-016) as the product formulation did not meet expected product profile;
- as a result of a proxy contest, new Board of Directors were elected at our annual meeting on September 22, 2008;

- in October 2008, our former Chief Executive Officer was relieved of his position. Our VP, Chief Financial Officer was appointed interim Chief Executive Officer; and
- in December 2008, a corporate restructuring plan was implemented to focus on growth opportunities and to conserve resources. The plan decreased the Company's personnel by approximately 35%.

Business Strategy

Our business strategy consists of the following three key pillars:

1. **Support and extend sales of AzaSite.** Working with our North American commercial partner, Inspire Pharmaceuticals, we will seek to increase AzaSite sales through a variety of approaches, including the evaluation of AzaSite for additional indications such as blepharitis, or inflammation of the eyelid. We are also seeking additional commercial partners outside the United States to market AzaSite in Japan and Europe.
2. **Develop and monetize our pipeline of ocular product candidates.** We plan to conduct preclinical and clinical testing of product candidates in our portfolio, and then partner with pharmaceutical companies to complete clinical development, manufacture, and market these products.
3. **Invest in long-term research and development opportunities.** We will seek to in-license or acquire promising product candidates and technologies from companies and academic institutions, then apply our expertise to create novel differentiated ophthalmic product opportunities. We may also utilize our DuraSite technology platform for the formulation of new ocular product candidates using either non-proprietary drugs or compounds originally developed by others for non-ophthalmic indications.

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.

Income Taxes. We account for income taxes in accordance with the provisions of Financial Accounting Standard Board ("FASB"), Statement of Financial Accounting Standard No. 109, " *Accounting for Income Taxes"* (SFAS 109) and Financial Interpretation No. 48, " *Accounting for Uncertainty in Income Taxes" — an interpretation of FASB Statement No. 109* (FIN 48). FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with 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.

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. For the year ended December 31, 2008, we generated net losses and, accordingly, did not record a provision for income taxes. As of December 31, 2008, our total deferred tax assets were $59.8 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. 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). 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.

We estimate the fair value of share-based awards on the date of grant using the Black-Scholes option-pricing method (Black-Scholes method). 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, 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. Our estimated volatility was derived using our historical stock price volatility. 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 $13.7 million, $23.8 million, and $2,000 for the years ended December 31, 2008, 2007 and 2006, respectively. $10.0 million of our revenues in 2008 primarily represented the non-cash amortization of the license fee for AzaSite. The amortization period for the license fee from Inspire for AzaSite ended in April 2008. $3.6 million of our revenues represented royalties from 2008 net sales of AzaSite by Inspire through December 31, 2008. The remaining revenue in 2008 represented contract services provided to Inspire related to its AzaSite activities. $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 were from sales of OcuGene.

Cost of revenues.

Our cost of revenues was $0.6 million, $1.0 million and $28,000 for 2008, 2007 and 2006, respectively. Cost of revenues for 2008 was comprised of royalties accrued for third parties, including Pfizer, based on the royalty report provided to us by Inspire. 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 reflected the cost of OcuGene tests performed as well as the cost of sample collection kits distributed for use.

Research and development.

Our research and development 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 2008, 2007 and 2006 (in thousands):

	As of December 31,		
	2008	2007	2006
Research	$ 7,286	$ 4,372	$3,291
Clinical development	8,956	6,012	5,599
Total research and development	$16,242	$10,384	$8,890

Research and development expenses were $16.2 million in 2008. In 2008, our activities primarily included the Phase 3(a) clinical trial of ISV-502, preparation for the production of Canadian AzaSite registration batches

at our contract manufacturing site, preclinical testing of AzaSite Otic, and preclinical experiments of ISV-405. Our activities related to the AzaSite Otic program were discontinued in July 2008 and our ISV-405 activities have been deferred.

Research and development expenses were $10.4 million in 2007. In 2007 our activities primarily included production of United States AzaSite process validation batches, expenses related to the AzaSite Canadian NDS filing, ISV-502 preclinical activities, Phase 1 clinical trial data evaluation, pilot study, Phase 3 clinical trial design and initiation and preclinical work on AzaSite Otic and ISV-405. Our research and development personnel costs were higher in 2007 due to success bonuses related to the successful FDA approval of AzaSite.

Research and development expenses were $8.9 million in 2006. In 2006, our activities had been primarily related to the AzaSite clinical trials, preparation of the related NDA and the FDA filing fee.

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 $8.3 million in 2008 from $6.8 million in 2007. This increase is primarily due to legal and other expenses related to our proxy contest.

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.

Severance.

Severance expenses were $1.9 million in 2008 which were associated with our corporate restructuring that occurred in 2008.

Interest, other income (expenses), net.

Interest expense and other income was an expense of $8.0 million, $100,000 and $1.5 million in 2008, 2007 and 2006, respectively. The increased expense in 2008 was primarily due to the interest expense on the $60 million non-convertible, non-recourse promissory notes issued (the “AzaSite Notes”) in February 2008 and related amortization of the debt issuance costs incurred from our issuance of the AzaSite Notes. The increase in interest expense was partially offset by the interest income on our higher cash and cash equivalents and short-term investments balance. The decreased expense in 2007 was primarily due to the repayment of short-term notes in February 2007. The expense in 2006 primarily reflects accrued interest payable on short-term notes and the accretion of the value of the debt discount related to the warrants issued as part of the note financing.

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. For the year ended December 31, 2008, we have financed our operations primarily from the issuance of the AzaSite Notes. At December 31, 2008, our unrestricted cash and cash equivalents were $37.5 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, 2008, cash used by operating activities was $29.5 million. For the year ended December 31, 2007 cash provided for operating activities was $18.2 million. In February 2007, the Company received a $32 million license and milestone payment from Inspire for AzaSite. In 2008, $9.9 million represented the non-cash amortization of the license fee and the remainder was amortized in 2007. For the year ended December 31, 2006, cash used for operating activities was $16.2 million.

Cash used in investing activities was $0.5 million, $1.0 million and $322,000, for 2008, 2007 and 2006, respectively, primarily related to cash outlays for additions to laboratory and other equipment.

Cash provided by financing activities was $55.8 million for 2008, reflecting the net proceeds from the issuance of the AzaSite Notes. Cash used in financing activities was $6.6 million for 2007, primarily due to the repayment of short-term notes payable in February 2007 and prepayment of debt issuance costs related to the AzaSite Notes. Cash provided by financing activities was $13.5 million for 2006, 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 2008 through 2006 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

Year	Net Proceeds
2008	$ 28,000
2007	$ 512,000
2006	$5.8 million

Cash Received from Private Placements of Equity Securities

Date	Net Proceeds	Shares of Common Stock Issued
August 2006	$5.8 million	4.8 million plus warrants to purchase 1.0 million shares

Cash Received from Private Placement of Notes

Date	Net Proceeds	Type of Notes	Interest Rates and Terms	Maturity Date
February 2008	$55.3 million	Long-Term Secured Notes	16% through May 15, 2019	May 15, 2019
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*

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

In February 2008, the Company's wholly-owned subsidiary, Azithromycin Royalty Sub, LLC completed a private placement of $60.0 million in aggregate principal amount of non-convertible, non-recourse promissory notes due in 2019. Net proceeds from the financing were approximately $55.3 million after transaction costs of approximately $4.7 million. In addition, $5.0 million of the proceeds was set aside for interest reserves. The annual interest rate on the notes is 16% with interest payable quarterly in arrears beginning May 15, 2008. The notes are secured by, and will be repaid from, royalties to be paid to the Company by Inspire Pharmaceuticals from sales of AzaSite in the United States and Canada. The secured notes payable are non-recourse to InSite

Vision Incorporated. 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. Any shortfall of interest payments from the royalty payments will be paid out of the interest reserves. As of December 31, 2008, no balance remained on the interest reserve. Further shortfalls, if any, can be paid by the Company at their option to avoid default under the agreement. The notes may be redeemed at the Company's option, subject to the payment of a redemption premium through May 2012. As of December 31, 2008, the $60.0 million of secured notes payable is classified as long-term.

In addition to the above, we received payments on a note from a stockholder of $168,000 in 2006.

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, ISV-502, 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 2009. 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.

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, 2008 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)	$ 40	$ 18	$ 22	$ —	$ —
Facilities Lease Obligations (2)	$ 3,997	754	1,574	1,669	
Licensing agreement obligations (3)	9,275	875	3,360	5,040	
Secured Notes Payable (4)	60,000		3,300	13,704	42,996
Interest Payments on Secured Notes Payable (5)	83,606	9,600	19,200	17,256	37,550
Total commitments	$156,918	$11,247	$27,456	$37,669	$80,546

(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) 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.

(4) Principal repayments are limited to royalties received from Inspire Pharmaceutical from sales of AzaSite in the United States and Canada. 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. Future payments represent an estimate of expected principal repayments based on minimum royalty income covered by the agreement. The note is due in 2019.
(5) Interest repayments represent an estimate based on expected principal repayments.

Recent Accounting Pronouncements

In December 2007, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standard No. 141 (revised 2007), "Business Combinations" (SFAS 141R). SFAS 141R expands the definitions of a business combination and includes the issuance of equity securities to be determined on the acquisition date, be recorded at fair value at the acquisition date; all assets, liabilities, contingent consideration, contingencies and in-process research and development costs of an acquired business be recorded at fair value at the acquisition date; acquisition costs generally be expensed as incurred; restructuring costs generally be expensed in periods subsequent to the acquisition date; and changes be made in accounting for deferred tax asset valuation allowances and acquired income tax uncertainties after the measurement period to impact income tax expense. Upon the Company's adoption of SFAS 141R, any subsequent changes to the Company's acquired uncertain tax positions and valuation allowances associated with acquired deferred tax assets will no longer be applied to goodwill, regardless of acquisition date of the associated business combination. Rather, those changes will typically be recognized as an adjustment to income tax expense. SFAS 141R applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. The adoption of this statement does not have an impact to the Company's consolidated financial position and results of operations, although would have an effect on reporting of any acquisitions completed after January 1, 2009.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 157, "Fair Value Measurements" (SFAS 157), which defines fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. In addition, SFAS 157 establishes a framework for measuring fair value and expands disclosure about fair value measurements. SFAS No. 157 is effective for fiscal years beginning after November 15, 2007 and interim periods within those years. However, in February 2008, the FASB issued FASB Staff Position ("FSP") FAS 157-1 and FSP FAS 157-2, which delayed the effective date of SFAS 157 for all nonrecurring fair value measurements of nonfinancial assets and nonfinancial liabilities, except those that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually) and removes certain leasing transactions from the scope of SFAS 157. FSP FAS 157-2 partially defers the effective date of SFAS 157 to fiscal years and interim periods beginning after November 15, 2008 for items within the scope of the FSP. The Company does not expect the adoption of FSP FAS 157-1 and FSP FAS 157-2 to have a material impact on the Company's consolidated financial position and results of operations.

In February 2007, the FASB issued Financial Accounting Standards No. 159, "Fair Value Option for Financial Assets and Financial Liabilities" (SFAS 159). SFAS 159 permits entities to choose to measure many financial instruments, and certain other items, at fair value. SFAS 159 also establishes presentation and disclosure requirements designed to facilitate comparisons between entities that choose different measurement attributes for similar types of assets and liabilities. The provisions of SFAS 159 are effective for fiscal years beginning after November 15, 2007. The Company adopted SFAS 159 and did not elect the fair value option for any of our eligible financial assets or liabilities.

In August 2008, the U.S. Securities and Exchange Commission, or SEC, announced that it will issue for comment a proposed roadmap regarding the potential use by U.S. issuers of financial statements prepared in accordance with International Financial Reporting Standards ("IFRS"). IFRS is a comprehensive series of accounting standards published by the International Accounting Standards Board, or IASB. Under the proposed

roadmap, the Company could be required in fiscal year 2014 to prepare financial statements in accordance with IFRS and the SEC will make a determination in 2011 regarding mandatory adoption of IFRS. The Company is currently assessing the impact that this potential change would have on our consolidated financial statements and will continue to monitor the development of the potential implementation of IFRS.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

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

The Company has long-term debt with fixed interest rates. As a result, our exposure to market risk caused by fluctuations in interest rates is minimal. Our borrowings outstanding as of December 31, 2008 was $60 million and the interest rate was 16%. If the market interest rates increased by 10% from the December 31, 2008 levels, it would not result in an increase in interest expense. As of December 31, 2008, the face value of our long-term debt approximates the fair value.

The securities in our investment portfolio are not leveraged and are subject to minimal interest rate risk. Due to their short-term nature, the securities are classified as cash and cash equivalents. Because of the short-term maturities of our investments, we do not believe that a change in market rates would have a significant negative impact on the value of our investment portfolio. While a hypothetical decrease in market interest rates by 10 percent from the December 31, 2008 levels would cause a decrease in interest income, it would not result in loss of principal.

The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. In the current economic environment to achieve this objective, we maintain our portfolio in cash equivalents, including obligations of U.S. government-sponsored enterprises and money market funds. These securities are classified as cash and cash equivalents and consequently are recorded on the balance sheet at fair value. We do not utilize derivative financial instruments to manage our interest rate risks.

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:

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, 2008 and 2007, 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, 2008. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The company is not required to have, nor have we been engaged to perform, an audit of the company's internal control over financial reporting. An audit includes consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion as of December 31, 2008. 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 financial statements referred to above present fairly, in all material respects, the consolidated financial position of InSite Vision Incorporated as of December 31, 2008 and 2007, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2008, in conformity with accounting principles generally accepted in the United States of America.

/s/ Burr, Pilger & Mayer LLP

San Francisco, California
March 13, 2009

INSITE VISION INCORPORATED

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share amounts)	December 31, 2008	December 31, 2007
ASSETS		
Current assets:		
Cash and cash equivalents	$ 37,456	$ 11,532
Restricted cash	—	75
Accounts receivable	1,455	719
Prepaid deal expenses	—	538
Prepaid expenses and other current assets	212	810
Total current assets	39,123	13,674
Property and equipment, at cost:		
Laboratory and other equipment	1,744	1,210
Leasehold improvements	292	289
Furniture and fixtures	177	160
	2,213	1,659
Accumulated depreciation	734	321
	1,479	1,338
Debt issuance costs, net	4,341	—
Total assets	$ 44,943	$ 15,012
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 1,162	$ 2,196
Accrued liabilities	729	853
Accrued compensation and related expense	638	979
Accrued royalties	326	57
Accrued interest	1,200	—
Deferred revenues	373	10,145
Total current liabilities	4,428	14,230
Capital lease obligation, less current portion	21	36
Secured notes payable	60,000	—
Total liabilities	64,449	14,266
Commitments and contingencies		
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value, 5,000,000 shares authorized, none issued and outstanding at December 31, 2008 and December 31, 2007	—	—
Common stock, $0.01 par value, 240,000,000 shares authorized; 94,681,618 issued and outstanding at December 31, 2008 and 94,585,449 issued and outstanding at December 31, 2007	947	946
Additional paid-in capital	148,384	147,327
Accumulated deficit	(168,837)	(147,527)
Total stockholders' equity (deficit)	(19,506)	746
Total liabilities and stockholders' equity (deficit)	$ 44,943	$ 15,012

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except per share amounts)	Year Ended December 31, 2008	2007	2006
Revenues:			
Licensing fee and milestone amortization	$ 9,972	$ 22,080	$ 2
Royalties	3,596	701	—
Other product and service revenues	138	980	—
Total	13,706	23,761	2
Cost of revenues	630	982	28
Gross profit (loss)	13,076	22,779	(26)
Operating expenses:			
Research and development(a)	16,242	10,384	8,890
General and administrative(a)	8,251	6,760	6,182
Severance	1,909		
Total	26,402	17,144	15,072
Income (loss) from operations	(13,326)	5,635	(15,098)
Interest (expense) and other income, net	(7,984)	(100)	(1,513)
Net income (loss)	$(21,310)	$ 5,535	$(16,611)
Net income (loss) per share:			
Earnings (loss) per share—basic	$ (0.23)	$ 0.06	$ (0.19)
Earnings (loss) per share—diluted	$ (0.23)	$ 0.06	$ (0.19)
Weighted average shares used in per-share calculation:			
—Basic	94,607	94,168	88,339
—Diluted	94,607	100,110	88,339
(a) Includes the following amounts related to stock based compensation:			
Research and development	$ 290	$ 282	$ 245
General and administrative	740	719	565

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

(in thousands, except per share amounts)	Preferred Stock		Common Stock		Additional Paid-in-Capital	Notes Receivable from Stockholders	Retained Earnings (Accumulated Deficit)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balances, December 31, 2005	—	$—	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 warrant	—	—	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)
Balances, December 31, 2006	—	—	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
Balances, December 31, 2007	—	—	94,585,449	946	147,327	—	(147,527)	746
Issuance of common stock from employee stock purchase plan	—	—	96,169	1	27	—	—	28
Employee stock compensation	—	—	—	—	1,018	—	—	1,018
Non-employee stock compensation	—	—	—	—	12	—	—	12
Net loss	—	—	—	—	—	—	(21,310)	(21,310)
Balances, December 31, 2008	—	$—	94,681,618	$947	$148,384	$ —	$(168,837)	$(19,506)

See accompanying notes consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2008	2007	2006
OPERATING ACTIVITIES:			
Net income (loss)	$(21,310)	$ 5,535	$(16,611)
Adjustment to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	413	236	97
Gain on sale of assets	(8)	(1)	—
Amortization of deferred debt issuance costs	361	22	809
Accretion of debt discount	—	—	798
Stock-based compensation	1,030	1,001	810
Changes in operating assets and liabilities:			
Accounts receivable	(736)	(719)	—
Prepaid expenses and other current assets	598	(15)	(697)
Accounts payable	(1,034)	1,819	(1,564)
Accrued liabilities	(124)	424	(786)
Accrued compensation and related expense	(341)	360	216
Accrued royalties	269	57	—
Accrued interest	1,200	(702)	699
Deferred revenues	(9,772)	10,145	—
Net cash provided by (used in) operating activities	(29,454)	18,162	(16,229)
INVESTING ACTIVITIES:			
Purchase of property and equipment	(554)	(1,013)	(322)
Proceeds from sale of asset	8	1	—
Restricted cash decrease	75	—	—
Net cash used in investing activities	(471)	(1,012)	(322)
FINANCING ACTIVITIES:			
Issuance of common stock from exercise of options, employee purchase plan and warrants, net of issuance costs	28	512	5,759
Issuance of common stock from private placement, net of issuance costs	—	—	5,810
Note payment received from stockholder	—	—	168
Issuance of short-term notes payable, net of issuance costs	—	—	1,783
Proceeds from issuance of secured notes payable	60,000		—
Payments for debt issuance costs	(4,164)	(538)	—
Repayments of borrowings	—	(6,300)	—
Payments of notes payable to related parties	—	(266)	—
Payment of capital lease obligation	(15)	(12)	(10)
Net cash (used in) provided by financing activities	55,849	(6,604)	13,510
Net increase (decrease) in cash and cash equivalents	25,924	10,546	(3,041)
Cash and cash equivalents at beginning of year	11,532	986	4,027
Cash and cash equivalents at end of year	$ 37,456	$11,532	$ 986
Supplemental disclosure of cash flow information:			
Interest received	$ 603	$ 8	$ 1
Interest paid	$ 7,045	$ 809	$ 16
Income taxes	$ 5	$ 1	$ 1
Non-cash investing and financing activities:			
Issuance of warrants to lenders in connection with notes payable	$ —	$ —	$ 307
Acquisition of property and equipment through capital lease	$ —	$ —	$ 71

See accompanying notes to consolidated financial statements.

InSite Vision Incorporated

Notes to Consolidated Financial Statements
December 31, 2008

1. Summary of Significant Accounting Policies

Basis of Presentation. The accompanying consolidated financial statements include the accounts of InSite Vision Incorporated and its wholly-owned subsidiaries ("InSite" or the "Company"). The Company 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 (deficit).

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. At December 31, 2007, prepaid deal expenses included $538,000 of expenses incurred related to the financing completed in February 2008. See Note 5, "Secured Notes Payable" for further discussion of this transaction.

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, 2008, 2007 and 2006 were $413,000, $236,000 and $97,000, 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.

Debt Issuance Costs. Debt issuance costs paid to third parties are capitalized and amortized over the life of the underlying debt, using the straight-line method. Amortization of debt issuance costs for the year ended December 31, 2008 was $361,000 and is included in interest expense and other income in the Consolidated Statements of Operations. See Note 5, "Secured Notes Payable" for further discussion of the underlying debt.

Fair Value Measurements. On January 1, 2008, the Company adopted Statement of Financial Accounting Standards ("SFAS") No. 157, "Fair Value Measurements" ("SFAS No. 157") which defines fair value, establishes a framework for using fair value to measure assets and liabilities, and expands disclosures about fair value measurements. SFAS No. 157 applies whenever other statements require or permit assets or liabilities to be measured at fair value. SFAS No. 157 is effective for fiscal years beginning after November 15, 2007, except for nonfinancial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a nonrecurring basis, for which application has been deferred for one year. The levels of fair value measurements defined in SFAS No. 157 are:

Level 1 Inputs are unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2 Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities. The Company had no Level 2 assets or liabilities at December 31, 2008.

Level 3 Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities. The Company had no material Level 3 assets or liabilities at December 31, 2008.

As of December 31, 2008, $37.1 million of our cash and cash equivalents consisted of Level 1 Treasury backed money market funds.

The Company's financial instruments consist mainly of cash equivalents, short-term accounts receivable, accounts payable and debt obligations. Short-term accounts receivable and accounts payable are reflected in the accompanying consolidated financial statements at cost, which approximates fair value due to the short-term nature of these instruments. While the Company believes its valuation methodologies are appropriate and consistent with other market participants, the use of different methodologies or assumptions to determine the fair value of certain financial instruments could result in a different estimate of fair value at the reporting date.

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 Expenses. Research and development 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.

The Company accounts for stock-based payments in accordance with 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.

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 11, "Employee Stock-Based Compensation" for further discussion of employee stock-based compensation.

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 $12,000, $22,000 and $6,000 during the years ended 2008, 2007 and 2006, 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 2008 and 2006 as their inclusion would be antidilutive.

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

	Year Ended December 31,		
(in thousands, except per share data)	2008	2007	2006
Numerator:			
Net income (loss)	$(21,310)	$ 5,535	$(16,611)
Denominator:			
Weighted-average shares outstanding	94,607	94,168	88,339
Effect of dilutive securities:			
Stock options and warrants	—	5,942	—
Weighted-average shares outstanding for diluted income (loss)	94,607	100,110	88,339
Net income (loss) per share:			
Basic	$ (0.23)	$ 0.06	$ (0.19)
Diluted	$ (0.23)	$ 0.06	$ (0.19)

For the years ended December 31, 2008 and 2006, 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, 2008, 2007 and 2006, 21,471,962, 1,016,957 and 23,412,320 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.

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, on January 1, 2007. 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 were from four AzaSite licensees. The Company is entitled to receive royalty revenue from net sales of AzaSite under the terms of its agreements with Inspire, Shin Poong, Biem, and Essex, 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 December 2007, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standard No. 141 (revised 2007), "Business Combinations" (SFAS 141R). SFAS 141R expands the definitions of a business combination and includes the issuance of equity securities to be determined on the acquisition date, be recorded at fair value at the acquisition date; all assets, liabilities, contingent consideration, contingencies and in-process research and development costs of an acquired business be recorded at fair value at the acquisition date; acquisition costs generally be expensed as incurred; restructuring costs generally be expensed in periods subsequent to the acquisition date; and changes be made in accounting for deferred tax asset valuation allowances and acquired income tax uncertainties after the measurement period to impact income tax

expense. Upon the Company's adoption of SFAS 141R, any subsequent changes to the Company's acquired uncertain tax positions and valuation allowances associated with acquired deferred tax assets will no longer be applied to goodwill, regardless of acquisition date of the associated business combination. Rather, those changes will typically be recognized as an adjustment to income tax expense. SFAS 141R applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. The adoption of this statement does not have an impact to the Company's consolidated financial position and results of operations, although would have an effect on reporting of any acquisitions completed after January 1, 2009.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 157, "Fair Value Measurements" (SFAS 157), which defines fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. In addition, SFAS 157 establishes a framework for measuring fair value and expands disclosure about fair value measurements. SFAS No. 157 is effective for fiscal years beginning after November 15, 2007 and interim periods within those years. However, in February 2008, the FASB issued FASB Staff Position ("FSP") FAS 157-1 and FSP FAS 157-2, which delayed the effective date of SFAS 157 for all nonrecurring fair value measurements of nonfinancial assets and nonfinancial liabilities, except those that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually) and removes certain leasing transactions from the scope of SFAS 157. FSP FAS 157-2 partially defers the effective date of SFAS 157 to fiscal years and interim periods beginning after November 15, 2008 for items within the scope of the FSP. The Company does not expect the adoption of FSP FAS 157-1 and FSP FAS 157-2 to have a material impact on the Company's consolidated financial position and results of operations.

In February 2007, the FASB issued Financial Accounting Standards No. 159, "Fair Value Option for Financial Assets and Financial Liabilities" (SFAS 159) . SFAS 159 permits entities to choose to measure many financial instruments, and certain other items, at fair value. SFAS 159 also establishes presentation and disclosure requirements designed to facilitate comparisons between entities that choose different measurement attributes for similar types of assets and liabilities. The provisions of SFAS 159 are effective for fiscal years beginning after November 15, 2007. The Company adopted SFAS 159 and did not elect the fair value option for any of our eligible financial assets or liabilities.

In August 2008, the U.S. Securities and Exchange Commission, or SEC, announced that it will issue for comment a proposed roadmap regarding the potential use by U.S. issuers of financial statements prepared in accordance with International Financial Reporting Standards ("IFRS"). IFRS is a comprehensive series of accounting standards published by the International Accounting Standards Board, or IASB. Under the proposed roadmap, the Company could be required in fiscal year 2014 to prepare financial statements in accordance with IFRS and the SEC will make a determination in 2011 regarding mandatory adoption of IFRS. The Company is currently assessing the impact that this potential change would have on our consolidated financial statements and will continue to monitor the development of the potential implementation of IFRS.

2. License Agreements

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.

In March 2008, the Company entered into a licensing and distribution agreement for AzaSite with Bioceutica S.A. in Argentina. Under the terms of the agreement, the Company granted exclusive rights to Bioceutica to commercialize AzaSite for ocular bacterial infection in Argentina, Chile, Paraguay and Uruguay.

In April 2008, the Company entered into a licensing and distribution agreement for AzaSite with Biem Pharmaceuticals in Turkey. Under the terms of the agreement, the Company granted exclusive rights to Biem Pharmaceuticals to commercialize AzaSite for ocular bacterial infection in Turkey.

In May 2008, the Company entered into a licensing and distribution agreement for AzaSite with Essex Bio-Technology in the People's Republic of China. Under the terms of the agreement, the Company granted exclusive rights to Essex to commercialize AzaSite for ocular bacterial infection in the People's Republic of China.

In all of these agreements, the licensee is responsible for obtaining regulatory approval and will generally pay the Company a double digit royalty on net sales of AzaSite in these countries, if approved by regulatory authorities. The Company will be responsible for providing AzaSite inventory to these licensees at a fee.

On February 15, 2007, the Company entered into a license agreement for AzaSite ™ 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 license 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, and (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 recognized the upfront license fee and milestone payment totaling $32 million ratably over the period that the Company was required to continue to provide services under the license agreement, which ended in April 2008, under the contingency-adjusted performance model of revenue recognition. During the years ended December 31, 2008 and December 31, 2007, the Company recognized $9.9 million and $22.1 million, respectively, 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 ISV-502 (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 year ended December 31, 2008 and December 31, 2007, the Company recorded third-party royalties of $629,000 and $122,000, respectively, due primarily under the Pfizer License.

3. Restricted Cash

As of December 31, 2007, 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 requirement for this restricted cash was eliminated in 2008.

As of December 31, 2008, the Company had no restricted cash or short-term investments.

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. The need for a bad debt allowance is evaluated each reporting period based on our assessment of the collectiblity of the amounts.

5. Secured Notes Payable

In February 2008, the Company's wholly-owned subsidiary, Azithromycin Royalty Sub, LLC completed a private placement of $60.0 million in aggregate principal amount of non-convertible, non-recourse promissory notes due in 2019. Net proceeds from the financing were approximately $55.3 million after transaction costs of approximately $4.7 million. In addition, $5.0 million of the proceeds was set aside for interest reserves. The annual interest rate on the notes is 16% with interest payable quarterly in arrears beginning May 15, 2008. The notes are secured by, and will be repaid from, royalties to be paid to the Company by Inspire Pharmaceuticals from sales of AzaSite in the United States and Canada. The secured notes payable are non-recourse to InSite Vision Incorporated. 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. Any shortfall of interest payments from the royalty payments will be paid out of the interest reserves. As of December 31, 2008, no balance remained on the interest reserve. Further shortfalls, if any, can be paid by the Company at their option to avoid default under the agreement. The notes may be redeemed at the Company's option, subject to the payment of a redemption premium through May 2012. As of December 31, 2008, the $60.0 million of secured notes payable is classified as long-term.

At December 31, 2008, the estimated future principal payments on the notes, based on minimum royalty income covered by the agreement, as follows (in thousands):

Year Ending December 31,	
2009	$ —
2010	—
2011	3,300
2012	5,548
2013	8,156
Thereafter	42,996
Total secured notes payable	60,000

6. Commitments and Contingencies

At December 31, 2008, the Company had contractual obligations of approximately $157.0 million, primarily related to the issuance of the AzaSite Notes (See Note 5) and minimum royalty payments related to license

agreements. These 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, 2008 and 2007 the Company had $71,000 of capital leased equipment with accumulated depreciation of $38,000 and $23,000, respectively.

Future minimum payments under capital leases are as follows:

Year Ending December 31,	Capital Leases
2009	$ 17,661
2010	17,661
2011	4,750
2012	—
2013	—
Total minimum lease payments	40,072
Amount representing interest	(4,404)
Present value of net minimum lease payment	35,668
Current Portion, in other current liabilities	(14,738)
Long-term portion	$ 20,930

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, 2008, 2007 and 2006, was $837,000, $695,000, and $706,000, respectively.

Year Ending December 31,	Operating Lease Cash Payments Required
2009	$ 754,132
2010	775,175
2011	798,483
2012	821,790
2013	847,528
2014 and thereafter	—
Total minimum lease payments	$3,997,108

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, 2008 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 2007 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, 2008 and 2007 are as follows (in thousands):

	2008	2007
Deferred tax assets:		
Net operating loss carryforwards	$ 38,150	$ 37,786
Tax credit carryforwards	6,520	5,637
Capitalized research and development	14,546	10,208
Depreciation	345	381
Other	252	300
Total deferred tax assets	59,813	54,312
Valuation allowance	(59,813)	(54,312)
Net deferred tax assets	$ —	$ —

During the year ended December 31, 2008, the valuation allowance increased by $5.5 million. During the year ended December 31, 2007, the valuation decreased by $5.5 million. During the year ended December 31, 2006, the valuation allowance increased by $6.6 million.

At December 31, 2008, the Company had net operating loss carryforwards for federal income tax purposes of approximately $98.2 million, which expire in the years 2009 through 2028 and federal tax credits of approximately $2.7 million, which expire in the years 2009 through 2028. At December 31, 2008, the Company also has net operating loss carryforwards for state income tax purposes of approximately $79.2 million which expire in the years 2009 through 2028 and state research and development tax credits of approximately $3.7 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 2006 for federal returns and 2005 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. Stockholders' Equity (Deficit)

In 2008, the Company received approximately $28,000 from the issuance of 96,169 shares acquired under the employee stock purchase plan

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
Total		$5,626,000	$162,000	9,207,452	8,676,132

The following table shows the detail of outstanding warrants as of December 31, 2008. 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
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	958,015	1.51	August 15, 2011	1,446,603
Total	15,257,936			11,704,760
Weighted-average exercise price per share				$ 0.77

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.

9. Employee Stock-based Compensation

The Company accounts for stock-based compensation in accordance with the provisions of 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 effect of recording stock-based compensation for the year ended December 31, 2008, 2007 and 2006 was as follows (in thousands):

	Year Ended December 31,		
	2008	2007	2006
Stock-based compensation expense by type of award:			
Employee stock options	$ 950	$ 936	$780
Employee stock purchase plan	68	43	24
Non-employee stock options	12	22	6
Total stock-based compensation	$1,030	$1,001	$810

Employee Stock-based Compensation

During the year ended December 31, 2008 and December 31, 2007, respectively, the Company granted options to purchase 630,250 and 1,071,001 shares of common stock with an estimated total grant date fair value of $0.2 million and $1.0 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, for the year ended December 31, 2008 and December 31, 2007, the Company estimated that the stock-based compensation for the awards not expected to vest was less than $0.1 million and $0.2 million, respectively. During the year ended December 31, 2008 December 31, 2007, and December 31, 2006, the Company recorded employee stock-based compensation related to all stock options of $950,000, $936,000, and $780,000, respectively.

As of December 31, 2008 and 2007, unrecorded deferred stock-based compensation balance related to stock options was $0.5 million and $1.8 million, respectively, and will be recognized over an estimate weighted-average amortization period of 1 year and 2.3 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. 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,	
	2008	2007
Risk-free interest rate	2.6% - 3.3%	3.3% - 4.6%
Expected term (years)	5%	5%
Expected dividends	0.0%	0.0%
Volatility	76.6%	74.8%

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, 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
Granted	630,250	0.47		
Exercised	—	0.00		
Canceled	(1,420,079)	1.19		
Outstanding at December 31, 2008	6,214,026	$1.00	3.67	$ 0
Options vested and exercisable and expected to be exercisable at December 31, 2008	6,058,685	$1.00	3.55	$ 0
Options vested and exercisable at December 31, 2008	5,287,717	$1.04	2.74	$ 0

At December 31, 2008, the Company had 4,671,043 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, 2008, 2007 and 2006 were $0.26, $0.91 and $1.52, respectively. The total intrinsic value of options exercised during the years ended December 31, 2007 and 2006 were $75,000 and $157,000, respectively.

The following table summarizes information concerning outstanding and exercisable options as of December 31, 2008:

	Option Outstanding			Options Vested and Exercisable	
		Weighted-Average			
Range of Exercise Prices	Number Outstanding	Contractual Life	Exercise Price	Number Exerisable	Weighted-Average Exercise Price
$0.36 - $0.52	635,000	8.02	$0.42	155,000	$0.41
$0.56 - $0.60	81,692	8.63	0.60	6,690	0.59
$0.63 - $0.63	1,784,382	3.09	0.63	1,734,421	0.63
$0.64 - $0.85	700,820	3.88	0.75	629,134	0.76
$0.88 - $1.13	806,272	1.91	1.01	783,172	1.01
$1.20 - $1.46	263,778	3.65	1.35	225,493	1.37
$1.50 - $1.50	1,240,420	3.31	1.50	1,132,515	1.50
$1.56 - $1.57	15,891	4.68	1.56	11,385	1.56
$1.59 - $1.59	630,000	3.17	1.59	554,136	1.59
$1.63 - $5.88	55,771	1.70	3.60	55,771	3.60
	6,214,026	3.67	$1.00	5,287,717	$1.05

At December 31, 2007 and 2006 options to purchase 4,629,501 and 3,720,567 shares of Common Stock were exercisable at weighted-average exercise prices of $1.01 and $1.25, 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, 2008 and December 31, 2007, respectively: risk-free interest rate of 3.0% and 3.7%; volatility factor of 73.8% and 74.4%; and an expected life of 1.5 years. During the year ended December 31, 2008 and December 31, 2007, the compensation cost in connection with the Purchase Plan was $68,000 and $43,000, respectively. During the year ended December 31, 2008 and December 31, 2007, 96,169 and 62,825 shares were issued under the Purchase Plan. As of December 31, 2008 and December 31, 2007, 571,965 and 543,134 shares were reserved for issuance under the Purchase Plan. As of December 31, 2008, the unrecorded deferred stock-based compensation balance related to the employee stock purchase plan was $29,000 and will be recognized over an estimated weighted average amortization period of 1.5 years.

10. Restructuring Charge

During the year ended December 31, 2008, the Company announced a corporate restructuring plan to focus on the Company's growth opportunities and conserve resources. The restructuring plan decreased the Company's personnel by 20 employees. In 2008, when the affected employees were notified of their termination, the Company estimated that severance related costs would total approximately $1.9 million which is recorded as

severance expense in the Consolidated Statement of Operations. As of December 31, 2008, $1.5 million of the severance has been paid and $0.2 million is a non-cash transaction related to the accelerated vesting of employee stock options. The remaining liability of $0.2 million, which is recorded accrued compensation and related expense in the Consolidated Balance Sheets, will be paid in 2009.

11. Legal Proceedings

The Company is subject to various claims and legal actions during the ordinary course of our business. We believe that there are currently no claims or legal actions that would have a material adverse impact on our financial position, operations or potential performance.

12. Quarterly Results (Unaudited)

The following table is a summary of the quarterly results of operations for the years ended December 31, 2008 and December 31, 2007. 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.

	2008			
(In thousands, except per share amounts)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	$ 7,931	$ 3,305	$ 960	$ 1,510
Cost of revenues	67	142	167	254
Income (loss) from operations	1,872	(3,442)	(5,625)	(6,131)
Net income/(loss)	970	(5,762)	(7,950)	(8,568)
—basic	$ 0.01	$ (0.06)	$ (0.08)	$ (0.09)
—diluted	$ 0.01	$ (0.06)	$ (0.08)	$ (0.09)

	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

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, 2008. 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, 2008, our internal control over financial reporting was effective.

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, 2008 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

(a) Information regarding our executive officers appears under the heading "Executive Officers of the Company" in Item 1 of Part I of this Annual Report on Form 10-K.

(b) The remaining 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 and such required information is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item will appear under the headings labeled "Director Compensation for 2008," "Compensation, Discussion and Analysis," "Compensation of Named Executive Officers," "Summary Compensation Table for 2008," "Grants of Plan Based Awards in 2008," "Outstanding Equity Awards at Fiscal 2008 Year End," " Option Exercises and Stock Vested in 2008," "Non-Qualified Deferred Compensation for 2008," "Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report" of our Proxy Statement and such required information is 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 such required information is 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 such required information is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Audit Fees

The information required by this Item will appear under the headings labeled "Audit Committee Matters" and "Principal Accounting Fees and Services" of our Proxy Statement and such required information is 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 Part II of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

The information required under this Item appears in the Financial Statements or notes thereto included in Item 8 of Part II 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

The information required under this Item appears under the heading "Exhibit Index" on page 63 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 13, 2009

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 Louis C. Drapeau, his or her attorneys in fact and agent, with the power of substitution and resubstition, for him or her and in his or her name, place and stead, in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys in fact, or his or her substitutes or agents, each acting alone, 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 below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Name	Capacity	Date
/s/ LOUIS C. DRAPEAU **Louis C. Drapeau**	Interim Chief Executive Officer and Chief Financial Officer (Principal Executive Officer and Principal Financial Officer)	March 13, 2009
/s/ RICK D. ANDERSON **Rick D. Anderson**	Director	March 13, 2009
/s/ TIMOTHY P. LYNCH **Timothy P. Lynch**	Director	March 13, 2009
/s/ TIMOTHY MCINERNEY **Timothy McInerney**	Director	March 13, 2009
/s/ EVAN S. MELROSE, M.D. **Evan S. Melrose, M.D.**	Director	March 13, 2009
/s/ ROBERT O'HOLLA **Robert O'Holla**	Director	March 13, 2009
/s/ ANTHONY J. YOST **Anthony J. Yost**	Director	March 13, 2009

EXHIBIT INDEX

Exhibit Index to InSite Vision Incorporated's Amendment No. 1 to its Annual Report on Form 10-K/A, as filed with the Securities and Exchange Commission on April 30, 2009.

Number	Exhibit Table
3.1[1]	Restated Certificate of Incorporation as filed with the Delaware Secretary of State on October 25, 1993
3.2[2]	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[2]	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[3]	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[4]	Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on June 3, 1994.
3.6[5]	Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on July 20, 2000.
3.7[5]	Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on June 1, 2004.
3.8[6]	Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on October 23, 2006
3.9[7]	Amended Bylaws, as amended on June 2, 2008.
4.1	Reference is made to Exhibits 3.1 through 3.9.
10.1[8]	InSite Vision Incorporated Amended and Restated Employee Stock Purchase Plan adopted October 15, 2007.
10.2[9HH]	InSite Vision Incorporated 1994 Stock Option Plan (Amended and Restated as of June 8, 1998).
10.3[8HH]	InSite Vision Incorporated 2007 Performance Incentive Plan.
10.4[8]	Form of Nonqualified Stock Option Agreement (2007).
10.5[8]	Form of Incentive Stock Option Agreement (2007).
10.6[10]	Form of Indemnification Agreement between the Company and its directors and officers.
10.7[11]	Form of Employee's Proprietary Information and Inventions Agreement.
10.8[12H]	License Agreement dated as of October 9, 1991 by and between the Company and CIBA Vision Corporation, as amended October 9, 1991.
10.9[13]	Facilities Lease, dated September 1, 1996, between the Registrant and Alameda Real Estate Investments.
10.10[14H]	Timolol Development Agreement dated July 18, 1996 by and between the Company and Bausch & Lomb Pharmaceuticals, Inc.
10.11[2H]	License Agreement, dated July 1, 1997, by and between the University of Connecticut Health Center and the Company.
10.12[2H]	License Agreement, dated August 19, 1997, by and between the University of Rochester and the Company.

Number	Exhibit Table
10.13[15]	Amendment No. 1 to Marina Village Office Tech Lease, dated July 20, 2001 and effective January 1, 2002.
10.14[16H]	License Agreement, dated December 21, 2001 by and between the Company and The University of Connecticut Health Center.
10.15[17H]	ISV-403 Asset Purchase Agreement, dated December 19, 2003, between the Company and Bausch & Lomb, Inc.
10.16[18]	Form of Class A Warrants issued under Subscription Agreement dated March 26, 2004.
10.17[18]	Form of Class B Warrants issued under Subscription Agreement dated March 26, 2004.
10.18[18]	Form of Placement Warrant issued pursuant to Placement Agreement dated February 12, 2004.
10.19[4]	Form of Common Stock Warrant issued under Subscription Agreement dated May 26, 2005.
10.20[4]	Form of Placement Agent Warrant, dated as of May 9, 2005.
10.21[19]	Warrant, dated as of October 6, 2005, for the purchase of 922,800 shares of Common Stock of the Company.
10.22[20]	Form of Warrant, dated as of January 11, 2006.
10.23[20]	Form of Placement Agent Warrant, dated as of January 11, 2006.
10.24[21]	Form of Warrant, dated as of August 15, 2006.
10.25[5]	Amendment No. 3 to Marina Village Office Tech Lease, dated November 28, 2006.
10.26[22H]	Exclusive License Agreement, dated as of February 15, 2007, by and between the Company and Pfizer, Inc. and Pfizer Products, Inc.
10.27[22H]	License Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.28[22H]	Trademark License Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.29[22H]	Supply Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.30[22HH]	Change in Control Agreement for S. Kumar Chandrasekaran adopted by InSite Vision Incorporated on May 2, 2007.
10.31[23]	Purchase and Sale Agreement, dated as of February 21, 2008, by and between Azithromycin Royalty Sub LLC and the Company.
10.32[23]	Note Purchase Agreement, dated as of February 21, 2008, by and among Azithromycin Royalty Sub LLC, the Company and the purchasers named therein.
10.33[23]	Indenture, dated as of February 21, 2008, by and between Azithromycin Royalty Sub LLC and U.S. Bank National Association.
10.34[23]	Pledge and Security Agreement made by the Company to U.S. Bank National Association, as Trustee, dated February 21, 2008.
10.35[23]	Residual License Agreement by and between Azithromycin Royalty Sub LLC and the Company dated February 21, 2008.
10.36[24]	InSite Vision Incorporated Annual Bonus Plan.
10.37[HH]	Offer Letter, dated as of October 31, 2008, by and between Interim CEO and the Company.

Number	Exhibit Table
22.1	List of Subsidiaries.
23.1*	Consent of Burr, Pilger & Mayer LLP, Independent Registered Public Accounting Firm.
24.1	Reference is hereby made to the Power of Attorney included on the signature page to the Company's Annual Report on Form 10-K for the year ended December 31, 2008.
31.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

1. Incorporated by reference to exhibits in the Company's Annual Report on Form 10-K for the year ended December 31, 1993.
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 in 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.
4. Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 (file Number 333-126084) as filed with the Securities and Exchange Commission on June 23, 2005.
5. Incorporated by reference to an exhibit in the Company's Annual Report on Form 10-K for the year ended December 31, 2006.
6. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2006.
7. Incorporated by reference to an exhibit in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 6, 2008.
8. 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.
9. 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.
10. 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.
11. Incorporated by reference to an exhibit in the Company's Annual Report on Form 10-K for the year ended December 31, 1993.
12. 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.
13. Incorporated by reference to an exhibit to the Company's Annual Report on Form 10-K for the year ended December 31, 1996.
14. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 1996.
15. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001.
16. Incorporated by reference to an exhibit to the Company's Annual Report on Form 10-K405 for the year ended December 31, 2001.
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 January 14, 2004.
18. 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.
19. 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).
20. 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).

21. 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).
22. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2007.
23. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2008.
24. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2008.
25. Incorporated by reference to an exhibit to the Company's Annual Report on Form 10-K for the year ended December 31, 2008.

* Filed herewith.

H Confidential treatment has been granted with respect to certain portions of this agreement.

HH Management contract or compensatory plan.

Exhibit 23.1

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 13, 2009, with respect to the consolidated financial statements which appear in this Form 10-K.

/s/ Burr, Pilger & Mayer LLP

San Francisco, California
March 13, 2009

EXHIBIT 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
AND 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)) 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 13, 2009

/s/ Louis C. Drapeau

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

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CORPORATE AND STOCKHOLDER INFORMATION

BOARD OF DIRECTORS

Evan S. Melrose, M.D.
Chairman of the Board
Managing Director, PTV Sciences

Rick D. Anderson
Managing Director, PTV Sciences

Timothy P. Lynch
General Partner, Stonepine Capital LLC

Timothy McInerney
Partner, Riverbank Capital Securities

Robert O'Holla
President, R.O.H. Consulting, LLC

Anthony J. Yost
General Manager, Western U.S.
Operating Unit, Novartis
Pharmaceuticals Corporation

EXECUTIVE TEAM

Louis Drapeau
Interim Chief Executive Officer and
Vice President, Chief Financial Officer

Lyle M. Bowman, Ph.D.
Vice President, Development

David Heniges
Vice President and General Manager,
Commercial Opportunities

Kamran Hosseini, M.D., Ph.D.
Vice President, Clinical Affairs and
Chief Medical Officer

Surendra Patel
Vice President, Operations

Corporate Headquarters
965 Atlantic Avenue
Alameda, CA 94501
tel: 510.865.8800
fax: 510.865.5700
mail@insitevision.com
www.insitevision.com

Corporate Counsel
O'Melveny & Myers LLP
Menlo Park, California

Independent Auditors
Burr, Pilger & Mayer, LLP
San Francisco, California

Transfer Agent and Registrar
American Stock Transfer
& Trust Company
Barry S. Rosenthal
Vice President
6201 15th Avenue
Brooklyn, NY 11219
tel: 718.921.8380
fax: 718.765.8718
www.amstock.com

Market Information

InSite Vision's common stock is listed on the Over-the-Counter Bulletin Board (OTCBB) under the symbol INSV and the sale price for a share of its common stock was $0.42 as of October 28, 2009.

InSite Vision has not paid any cash dividends on its common stock and does not intend to do so in the foreseeable future.

All exhibits to the Company's Annual Report on Form 10-K/A are briefly described in the exhibit table of that form, a copy of which is included herewith. The Company will provide stockholders with copies of any exhibits to the Company's Annual Report upon receipt of a written request at Investor Relations, 965 Atlantic Avenue, Alameda, California 94501 or by telephone to (510) 865-8800.

This Annual Report contains certain forward-looking statements that involve risks and uncertainties, such as statements of our plans, beliefs, objectives, expectations and intentions. Actual results or events could differ materially from those discussed herein. Factors that could cause or contribute to such differences include those discussed under "Risk Factors" and elsewhere in our Annual Report on Form 10-K included herewith and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009. The cautionary statements made in these documents should be read as applicable to all related forward-looking statements wherever they appear in this document and the enclosures included herewith. Readers are cautioned not to place undue reliance on these forward-looking statements, which are based on the limited information currently available to us and are subject to change. Although any such forward-looking statements or projections and the factors influencing them will likely change, 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.

INSITE VISION INCORPORATED

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www.insitevision.com

InSiteVision

Solutions for Sight