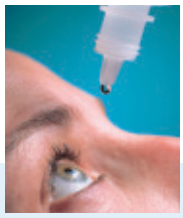
InSiteVision

Solutions for Sight

2012 Annual Report

OUR VISION



We aspire to be the leading global ophthalmic therapeutics company for front-of-eye conditions.

InSite Vision is advancing new ophthalmologic products for unmet eye care needs based on its innovative **DuraSite®** platform technologies. The **DuraSite®** and **DuraSite® 2** drug delivery systems extend the duration of drug retention on the surface of the eye, thereby reducing the frequency of treatment and improving the efficacy of topical drugs.

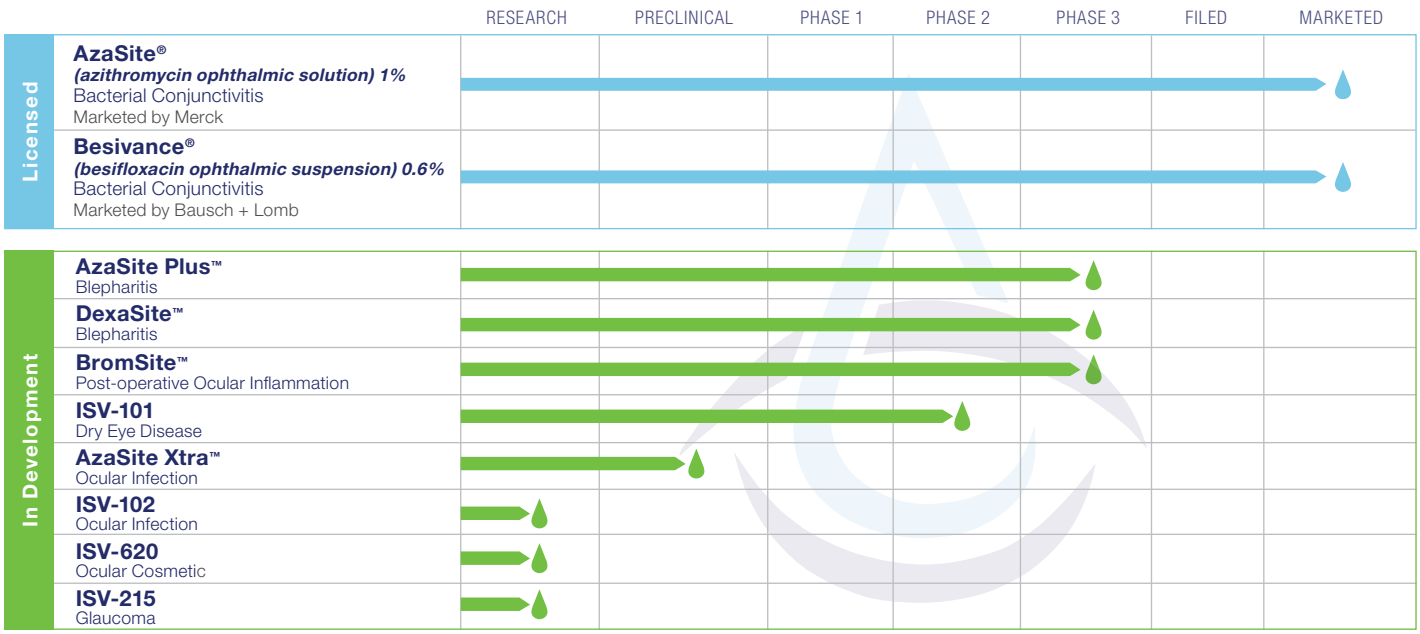
The **DuraSite®** platform is currently leveraged in two commercial products for the treatment of bacterial eye infections, **AzaSite®** (azithromycin ophthalmic solution) 1%, marketed in the U.S. by Merck, and **Besivance®** (besifloxacin ophthalmic suspension) 0.6%, marketed worldwide by Bausch + Lomb.

InSite Vision is simultaneously advancing three novel ophthalmic therapeutics through Phase 3 clinical studies: **AzaSite Plus™** and **DexaSite™** for the treatment of blepharitis, and **BromSite™** for pain and inflammation associated with cataract surgery.

"Our goal is to build value for our shareholders by advancing novel ophthalmic therapeutics, and we are incredibly optimistic about the prospects for InSite Vision. This year, we are reporting data from pivotal studies conducted in 2012 for three wholly owned Phase 3 product candidates. At the same time, we continue to build off our core DuraSite platform technology to innovate novel ophthalmic therapeutics."

– Timothy M. Ruane, CEO

PRODUCT PIPELINE



AzaSite Plus™	DexaSite™	BromSite™
A fixed-dose combination of an antibiotic and an anti-inflammatory steroid formulated with **DuraSite®** for the treatment of blepharitis	A **DuraSite®** formulation of dexamethasone for the treatment of ocular inflammation, including blepharitis	A low-dose NSAID formulated in **DuraSite®** for the treatment of inflammation and ocular pain following cataract surgery
Data from the Phase 3 DOUBle clinical study evaluating **AzaSite Plus™** and **DexaSite™** for the treatment of blepharitis is expected by midyear		**BromSite™** achieved statistically significant superiority compared to vehicle in reducing post-surgical inflammation and pain in a Phase 3 study

FORM 10-K

2012 ANNUAL REPORT

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, 2012

OR

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

Commission file number: 0-22332

INSITE VISION INCORPORATED

(Exact name of registrant as specified in its charter)

Delaware	**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:
None

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

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.01 par value per share	OTC Bulletin Board

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 whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 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, 2012 was approximately $28,152,000 (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 19, 2013: 131,951,033.

Portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission in connection with its 2013 annual meeting of stockholders are incorporated by reference into Part III hereof.

ANNUAL REPORT ON FORM 10-K
FOR THE YEAR ENDED DECEMBER 31, 2012

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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 under "Risk Factors," and 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. References in this Annual Report on Form 10-K to the "Company," "InSite," "we," "our" and "us" refer to InSite Vision, Incorporated and its consolidated subsidiaries, unless we state, or the context indicates, otherwise.

PART I

Item 1. Business

THE COMPANY

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

Our DuraSite sustained drug delivery technology is a proven synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a drug as a solution, gel or suspension and can be customized for delivering a wide variety of drug candidates. We have focused our research and development and commercial support efforts on the following topical products formulated with our DuraSite drug delivery technology.

- AzaSite® (azithromycin ophthalmic solution) 1% is a DuraSite formulation of azithromycin, a broad spectrum ocular antibiotic approved by the U.S. Food and Drug Administration (FDA) in April 2007 to treat bacterial conjunctivitis (pink eye). It was commercialized in the United States by Inspire Pharmaceuticals, Inc. (Inspire) beginning in August 2007. The key advantages of AzaSite are a significantly reduced dosing regimen leading to better compliance and outcome, a trusted broad spectrum antibiotic, and a lowered probability of bacterial resistance based on high tissue concentration. In May 2011, Merck & Co. (Merck) acquired Inspire and Inspire became a wholly-owned subsidiary of Merck. Merck is now responsible for commercializing AzaSite in North America. We receive a 25% royalty on net sales of AzaSite in North America, plus minimum royalties if applicable.
- Besivance® (besifloxacin ophthalmic suspension) 0.6% is a DuraSite formulation of besifloxacin, a broad spectrum ocular antibiotic approved by the FDA in May 2009 to treat bacterial conjunctivitis (pink eye). An advantage of Besivance is a faster rate of resolution of the infection that may reduce the duration of the illness and reduce the chances of infecting others. Besivance was developed by Bausch + Lomb Incorporated (Bausch & Lomb) and launched in the United States in the second half of 2009. In 2011, Besivance was launched internationally in select countries. We receive a middle single-digit royalty on net sales of Besivance globally.
- AzaSite Plus™ (ISV-502) is a fixed combination of azithromycin and dexamethasone in DuraSite for the treatment of ocular inflammation and infection (blepharitis and/or blepharoconjunctivitis) for which there is no FDA approved indicated treatment. We completed a Phase 3 trial in November 2008 for the treatment of blepharoconjunctivitis and AzaSite Plus was very well tolerated. Although efficacious, the trial did not achieve its primary clinical endpoint as defined by the previous protocol. We discussed the results of this trial with the FDA and determined a new development plan for this product candidate. In May 2011, we reached an agreement with the FDA on a Special Protocol Assessment (SPA) for the

design of a Phase 3 clinical trial of AzaSite Plus in patients with blepharitis. An SPA is a written agreement with the FDA that the study design and planned analysis of the sponsor's Phase 3 clinical trial adequately addresses the objectives necessary to support a regulatory submission. In November 2011, we initiated a new Phase 3 clinical trial for this product candidate in blepharitis and completed patient enrollment in the clinical trial in September 2012. This study enrolled more than 900 patients and we expect to receive top-line data in the second quarter of 2013.

- DexaSite™ (ISV-305) is a DuraSite formulation of dexamethasone in development for the treatment of ocular inflammation. DexaSite is included in the Phase 3 clinical trial SPA for AzaSite Plus. In November 2011, we initiated a Phase 3 clinical trial for this product candidate in blepharitis and completed patient enrollment in the clinical trial in September 2012. This study enrolled more than 900 patients and we expect to receive top-line data in the second quarter of 2013.
- BromSite™ (ISV-303) is a DuraSite formulation of bromfenac in development for the treatment of post-operative inflammation and eye pain. We initiated a Phase 1/2 clinical trial for this product candidate in August 2010 and we received positive top-line results from this study in the first quarter of 2011, which demonstrated the efficacy and safety of BromSite. In the third quarter of 2011, we completed an additional Phase 2 clinical trial to investigate the pharmacokinetics (PK) of BromSite in humans. We received positive top-line results that showed that the mean concentration of bromfenac in the aqueous humor of patients using BromSite was more than double compared to the currently available bromfenac eye product. In July 2012, we initiated a Phase 3 clinical trial for this product candidate and completed patient enrollment in November 2012 with 268 patients enrolled. In March 2013, we received positive top-line results that demonstrated a reduction of inflammation and pain after cataract surgery at a lower drug concentration compared to the current market leader.
- DuraSite 2® is our next-generation enhanced drug delivery system, which is designed to provide a broad platform for developing superior ophthalmic therapeutics. DuraSite 2 is based on the original DuraSite technology, and incorporates a cationic polymer to achieve sustained and enhanced ocular delivery of drugs. DuraSite 2 is designed to increase the tissue penetration for topically delivered ocular drugs with the aim of improved efficacy and dosing convenience. We obtained preclinical data from a comparative study that demonstrated superior drug retention and tissue penetration compared to DuraSite. We plan to utilize the DuraSite 2 platform in future pipeline product candidates and expect that it will be available for license for our other drugs. A patent application for DuraSite 2 was submitted to the U.S. Patent and Trademark Office (USPTO) in 2009.
- ISV-101 is a DuraSite formulation with a low concentration of bromfenac for the treatment of dry eye disease. We filed an Investigational New Drug Application (IND) with the FDA for this product candidate in the first quarter of 2011. We plan to initiate a Phase 1/2 clinical trial for this product candidate, but no time period has been set.

Business Strategy.

Our business strategy consists of the following:

1. Develop our pipeline of ocular product candidates. We seek to identify new product candidates from proven drugs that can be improved by formulation in DuraSite, which can substantially reduce the clinical risk involved in these product candidates. As appropriate, we plan to conduct preclinical and clinical testing of our product candidates.

2. Partner our product candidates. When we deem it appropriate, we seek to partner with larger pharmaceutical companies to manufacture and market our products. Partnering agreements generally include upfront and milestone payments, as well as on-going royalty payments upon commercialization, payable to us.

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 (SEC). Additionally, copies of materials filed by us with the SEC may be accessed at the SEC's Public Reference Room at 100 F Street NE, Washington D.C. or at the SEC's website at http://www.sec.gov. For information about the SEC's Public Reference Room, the public may contact 1-800-SEC-0330.

Ophthalmic Anti-Infective Market

The ocular anti-infectives market is estimated at $1.4 billion. Eye infections are routinely treated with topical antibiotics or antibiotic/corticosteroid fixed combination products. We are developing topical products to treat eye and eye-lid infections and/or inflammations. Some of these infections and/or inflammations are either under-treated or do not have an FDA-approved product indication. These infections and/or inflammations can be both acute and chronic. Our goal is to provide highly effective, safe 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, or where we believe our product candidates are well-suited to improving patient care:

- *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. Approximately four million cases of bacterial conjunctivitis are seen annually in the United States in children and adults, with direct and indirect costs estimated to be as much as $857 million annually. The conjunctiva is the transparent lining on the inside of the eyelids and the white part of the eye. In bacterial conjunctivitis, bacteria infects these parts of the eye and the white part of the eye may look pink from the inflammation. As it is an extremely contagious condition, immediate treatment is recommended. Our developed ocular antibiotics, AzaSite and Besivance, are targeted at treating this disease with significantly lower dosing than competing products.
- *Eye-lid Infections*.
  - *Blepharitis* (also known as lid margin disease) is a chronic inflammation of the eyelids, particularly the eyelid margins where the eyelashes grow. It is a common disorder, particularly among the elderly, that may be caused by bacterial growth, viral infection, allergies, environmental conditions or systemic disease. In a survey conducted by researchers at George Washington University, ophthalmologists and optometrists reported that blepharitis is commonly seen in the clinical practice in 37% and 47% of their patients, respectively. In spite of that frequency, blepharitis is frequently misdiagnosed or under-diagnosed.

    Blepharitis is a chronic condition with periodic acute episodes that are difficult to treat. An eyelid with blepharitis may become itchy and appear red and swollen with scaly, greasy debris along the lid margin. There are no approved pharmaceutical products for the treatment of blepharitis. Patients are typically advised to use lid scrubs, hot compresses, lid massage, antibiotics, corticosteroids and fixed-combination products. We are conducting a Phase 3 clinical trial of two novel ophthalmic products that utilize our DuraSite drug delivery technology to alleviate the signs and symptoms of blepharitis; AzaSite Plus, a topical anti-bacterial and anti-inflammatory combination product; and DexaSite, a corticosteroid anti-inflammatory agent.
  - *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 and 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. Typical treatment includes eye hygiene using lid scrubs, topical and/or systemic antibiotics and topical corticosteroids.

Ocular Inflammation and Pain Market

We are developing novel ophthalmic therapeutics for the treatment of conditions associated with ocular inflammation. These efforts are initially focused on two indications, post-operative inflammation and pain, and dry eye disease.

- *Post-Operative Ocular Inflammation and Pain* is typically treated using non-steroidal anti-inflammatory drugs (NSAIDs). An estimated 60 percent of ophthalmic surgeons deploy topical NSAIDs before and after cataract and other procedures to address patient pain and prevent complications, such as cystoid macular edema. Cystoid macular edema (CME) is a serious post-surgical complication that occurs when inflammation and swelling develop in the center of the retina. Although rare, it is the most common cause of decreased vision or even blindness following cataract surgery. Cataract surgery is the most frequent ophthalmic procedure conducted in the United States, with approximately 3 million cataract surgeries performed annually. The ophthalmic NSAID market is estimated to be $320 million, with more than 2.6 million prescriptions written annually. As the population in the U.S. ages, the market for ocular NSAIDs that are effective and easy for patients to use is expected to grow 7.1 percent between 2007 and 2014. We completed a Phase 3 clinical study of our BromSite product candidate, which is intended to relieve post-operative ocular inflammation and pain while providing superior tissue penetration of drug to the eye that may reduce the incidences of CME with convenient twice-daily dosing.
- *Dry Eye Disease* occurs when the ocular surface and/or tear film is compromised. While causes of dry eye may vary, it is frequently associated with inflammation of the surface of the eye, the lacrimal gland, or the conjunctiva. A chronic condition that can occur at any age, dry eye disease is most prevalent among the elderly. Symptoms of dry eye disease include a scratchy feeling as if something is in the eye, stinging or burning of the eye; episodes of excess tearing that follow periods of very dry sensation; stringy discharge from the eye and pain or redness. According to the National Eye Institute, dry eye disease is estimated to affect five million people age 50 and older in the U.S. alone, with tens of millions more experiencing less severe symptoms. We have developed a low-dose topical NSAID, known as ISV-101, intended for the treatment of dry eye disease. We plan to initiate a Phase 1/2 clinical trial for ISV-101, but no time period has been set.

Products and Product Candidates

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

Principal DuraSite Products and Product Candidates
Active Programs

Product	Indications	Anticipated Benefits	Status
AzaSite	Bacterial conjunctivitis (pink eye)	Broad-spectrum macrolide antibiotic with reduced dosing frequency	*Approved and launched in U.S. *Approved in Canada
Besivance	Bacterial conjunctivitis (pink eye)	Broad-spectrum fluoroquinolone antibiotic with reduced dosing frequency	*Approved and launched in the U.S. and select countries internationally
AzaSite Plus	Blepharitis	Broad-spectrum antibiotic combined with a potent corticosteroid with reduced dosing frequency to treat both inflammation and infection	Phase 3 clinical trial patient enrollment completed
DexaSite	Ocular inflammation	A potent corticosteroid with reduced dosing frequency to treat inflammation	Phase 3 clinical trial patient enrollment completed
BromSite	Post-operative inflammation and eye pain	A non-steriodal anti-inflammatory to treat pain and inflammation	Phase 3 clinical trial completed
ISV-101	Dry eye disease	A low dose non-steriodal anti-inflammatory to treat dry eye disease	Filed an IND with the FDA Phase 1/2 clinical trial planned

The DuraSite Product Family of Topical Anti-infectives and Product Candidates

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

We 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 and the white part of the eye. 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 twice-a-day dosing 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 effective. AzaSite was approved by the FDA in April 2007. In August 2007, Inspire Pharmaceuticals commercially launched AzaSite in the United States pursuant to its license from InSite. In May 2011, Merck acquired Inspire and Inspire became a wholly-owned subsidiary of Merck. AzaSite is commercialized by Merck in the United States.

Besivance: Launched commercially in the United States by Bausch & Lomb in second half of 2009 for Bacterial Conjunctivitis (pink eye) and now available in select countries internationally

Besivance (besifloxacin ophthalmic suspension) 0.6% is indicated for the treatment of bacterial conjunctivitis in patients one year or older and is marketed by Bausch & Lomb.

Besivance is the first fluoroquinolone specifically developed for ophthalmic use and is the first and only ophthalmic fluoroquinolone with no previous systemic use. It offers broad-spectrum antibacterial activity, including activity against the strains that are the most common causes of bacterial conjunctivitis.

In clinical trials, investigators found that Besivance treatment resulted in a greater proportion of patients experiencing clinical resolution and microbial eradication when compared to its vehicle.

Besivance was approved by the FDA in May 2009. The product was launched commercially in the second half of 2009 in the United States. In 2011, Besivance was launched internationally in select countries.

AzaSite Plus: Phase 3 Clinical Trials for Blepharitis/Blepharoconjunctivitis

Expansion of our AzaSite product into a larger franchise includes a fixed combination of azithromycin with dexamethasone for the treatment of blepharitis/blepharoconjunctivitis, an infection of the eyelid and the conjunctiva, as well as other ophthalmic infections. In 2006, we completed our preclinical development of this combination product candidate, filed an 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 clinical trial indicated that AzaSite Plus 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 AzaSite Plus group and placebo group after 14 days of treatment.

In the fall of 2007, we conducted a pilot study to evaluate endpoints and time points for use in the Phase 3 trial for AzaSite Plus. 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 trial, which included lid margin redness, lid swelling, conjunctival redness, ocular discharge and lid irritation in at least one eye.

The Phase 3 trial tested a total of 417 patients with blepharoconjunctivitis. The dosing regimen consisted 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 AzaSite Plus in treating blepharoconjunctivitis over AzaSite alone or DexaSite alone.

Results from the Phase 3 trial indicated that AzaSite Plus improved clinical outcomes as compared to treatment with AzaSite alone in the reduction of inflammatory signs and symptoms and dexamethasone alone in bacterial eradication. AzaSite Plus was very well tolerated. However, an evaluation of the data indicated that the trial did not achieve its primary clinical endpoint as the reduction of inflammatory signs and symptoms between AzaSite Plus and DexaSite was statistically equivalent.

In April 2009, we discussed the results of this trial with the FDA and, based on this meeting, we developed a protocol for the treatment of blepharitis that would seek to demonstrate AzaSite Plus's ability to delay exacerbation and/or recurrence of acute episodes of blepharitis. This study would serve as a basis for revisions to the pivotal Phase 3 clinical trial protocols.

In 2010, we discussed a development pathway for this product candidate with the FDA. In May 2011, we reached an agreement with the FDA on a SPA for the design of a Phase 3 clinical trial of AzaSite Plus in patients with blepharitis. The trial design includes four study arms to receive AzaSite Plus, DexaSite, AzaSite or the DuraSite vehicle twice-daily for a period of 14 days. Under the SPA-approved trial protocol, AzaSite Plus was evaluated for safety and efficacy against AzaSite for the primary clinical endpoint of resolution of the clinical signs and symptoms of blepharitis and against DexaSite to compare the length of time to recurrence or exacerbation of symptoms following the treatment period. AzaSite Plus was also evaluated for the secondary clinical endpoint of clinical improvement of signs and symptoms of blepharitis against AzaSite. In November 2011, we initiated a Phase 3 clinical trial for this product candidate and completed patient enrollment in the clinical trial in September 2012. This study enrolled more than 900 patients and we expect to receive top-line data in the second quarter of 2013.

DexaSite: A second candidate for blepharitis in Phase 3 development

We developed a topical formulation of the corticosteroid dexamethasone to treat eye inflammation caused by infections, injury, surgery or other conditions. In 2007, we completed our preclinical development of this product candidate. This is a second product candidate originating from the IND filed for AzaSite Plus.

In 2008, the data from our Phase 3 clinical trial indicated that DexaSite was efficacious and well tolerated with no serious adverse events. Treatment-related ocular adverse events were minimal in frequency and equivalent between all groups. There were no significant differences in intraocular pressure between the DexaSite group and the other group containing dexamethasone after 14 days of treatment.

In 2010, we discussed a development pathway for this product candidate with the FDA. DexaSite was included in the Phase 3 clinical trial SPA for AzaSite Plus, which allows us to simultaneously evaluate both agents in a single Phase 3 clinical trial for the treatment of blepharitis. Per the SPA-approved protocol, the efficacy and safety of DexaSite was measured against the DuraSite vehicle for the primary clinical endpoint of resolution of clinical signs and symptoms of blepharitis at the end of the dosing period. DexaSite was also evaluated for the secondary clinical endpoint of clinical improvement of signs and symptoms of blepharitis. In November 2011, we initiated a Phase 3 clinical trial for this product candidate and completed patient enrollment in the clinical trial in September 2012. This study enrolled more than 900 patients and we expect to receive top-line data in the second quarter of 2013.

BromSite: Phase 3 clinical trial for post-operative inflammation and eye pain completed

We developed a topical formulation of the non-steriodal anti-inflammatory bromfenac to treat post-operative inflammation and eye pain in patients who have undergone cataract surgery. In the first half of 2010, we completed our preclinical development of this product candidate and filed an IND with the FDA. In the second half of 2010, we initiated and completed enrollment for the Phase 1/2 clinical trial for this product candidate. In the first quarter of 2011, we received positive top-line results from this study, which demonstrated the efficacy and safety of BromSite. In the third quarter of 2011, we completed an additional Phase 2 clinical trial to investigate the PK of BromSite in humans. We received positive top-line results that showed that the mean concentration of bromfenac in the aqueous humor of patients using BromSite was more than double compared to the currently available bromfenac eye product. We discussed the design of the Phase 3 clinical trial with the FDA. The BromSite Phase 3 clinical study was a two-arm, double-blind, placebo-controlled clinical trial where the placebo arm was the DuraSite vehicle. Patients undergoing cataract surgery were randomized and then dosed twice-a-day beginning the day before surgery and continuing the day of surgery and 14 days post-surgery. The primary study endpoint is the reduction of pain and inflammation after surgery. In July 2012, we initiated a Phase

3 clinical trial for this product candidate and completed patient enrollment in November 2012 with 268 patients enrolled. In March 2013, we received positive top-line results that demonstrated a reduction of inflammation and pain after cataract surgery at a lower drug concentration compared to the current market leader.

ISV-101: Filed an IND for this product candidate

We developed a topical formulation of the non-steriodal anti-inflammatory bromfenac to treat dry eye disease. In January 2011, we filed an IND with the FDA. We plan to initiate a Phase 1/2 clinical trial for this product candidate, but no time period has been set.

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 synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a drug as 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 is designed to result 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 DuraSite 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, demonstrates sustained release and is 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 DuraSite. DuraSite has been used commercially in AquaSite, an ophthalmic product for dry eye syndrome; AzaSite, a topical anti-infective product for the treatment of bacterial conjunctivitis; and Besivance, besifloxacin ophthalmic suspension, 0.6%.

DuraSite 2 is our next-generation enhanced drug delivery system, which is designed to provide a broad platform for developing superior ophthalmic therapeutics. DuraSite 2 is based on the original DuraSite technology, and incorporates a cationic polymer to achieve sustained and enhanced ocular delivery of drugs. DuraSite 2 is designed to increase the tissue penetration for topically delivered ocular drugs with the aim of improved efficacy and dosing convenience. We have preclinical data from a comparative study that demonstrated superior drug retention and tissue penetration compared to DuraSite. We plan to utilize the DuraSite 2 platform in future pipeline product candidates and expect that it will be available for license for our other drugs. A patent application for DuraSite 2 was submitted to the USPTO in 2009.

Additional Research and Development Opportunities

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

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 agreements. 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 or renewed or that they will not be terminated.

Pfizer and Pfizer Products, Inc. In February 2007, we entered into a worldwide, exclusive, royalty-bearing licensing agreement with Pfizer (Pfizer License) under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus. Under the Pfizer License, we are required to pay Pfizer a 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. We have the right to grant sublicenses, subject to Pfizer's prior approval which shall not be unreasonably withheld.

Merck. In February 2007, we entered into a license agreement with Inspire. In May 2011, Merck acquired Inspire and Inspire is currently a wholly-owned subsidiary of Merck. Under the license agreement (Merck License), 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 Merck 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 Merck an exclusive sublicense under the Pfizer patent rights that we have licensed under the Pfizer License discussed above. Merck has the right to grant sublicenses under the terms of the Merck License.

Under the Merck License, Inspire paid us license fees and a milestone payment totaling $32 million through FDA approval in April 2007. Merck also pays us a royalty on net sales. The royalty rate is 25%. Merck is obligated to pay us royalties under the Merck License for the longer of (i) eleven years from the launch of the first product (August 13, 2007) or (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, Merck is required to pay us the greater of the royalty discussed above or certain tiered minimum royalties, which minimum royalties will terminate in September 2013. The minimum royalty for the fiscal year ending September 30, 2013 is $19 million, payable on a quarterly basis. The royalties under the Merck License are subject to certain reductions in the event of patent invalidity, third party licenses, generic competition and uncured material breach.

After obtaining regulatory approval in the United States and Canada, we transferred all regulatory documentation regarding AzaSite to Merck. Thereafter, Merck has been responsible for all regulatory obligations and strategies relating to the further development and commercialization of products in the United States and Canada. Merck is also responsible for commercialization in both the U.S. and Canada.

We also entered into a trademark license agreement with Merck in February 2007 under which we granted Merck 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 United States and Canada under the terms of the Merck License.

We also entered into a supply agreement (Supply Agreement) with Merck in February 2007 for azithromycin. We had previously entered into a third-party supply agreement for the production of azithromycin. The Supply Agreement was terminated in July 2012.

During the years ended December 31, 2012, 2011 and 2010, Merck royalties and supply revenues represented approximately 90%, 90% and 92%, respectively, of our total revenues.

Catalent Pharma Solutions, formerly Cardinal Health PTS, L.L.C. The AzaSite NDA was transferred to Merck and manufacturing responsibilities for AzaSite were transferred to Merck for sales in the United States and Canada. We continue to have a relationship with Catalent for the manufacture of AzaSite for sales outside the U.S. and Canada and for research and development purposes, as well as for other products in our pipeline.

Bausch and Lomb Incorporated. In December 2003, we completed the sale of a drug candidate for the treatment of ocular infections to Bausch & Lomb pursuant to a purchase agreement and a license agreement (License Agreement) (collectively, the Asset Sale). The drug candidate, Besivance, was developed by Bausch & Lomb. In May 2009, the FDA approved Besivance to treat bacterial conjunctivitis (pink eye). Besivance was launched in the United States by Bausch & Lomb in 2009. In 2011, Besivance was launched internationally in select countries.

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

The License Agreement provides Bausch & Lomb a license to certain of our patents related to our DuraSite delivery system for use with Besivance and to other non-patented intellectual property used in Besivance. 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.

Other. 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, six U.S. patents have been issued. We have four U.S. patents on our retinal drug delivery device that have been issued. Six U.S. patents have been issued related to our antibiotic programs with two applications pending. At least eight 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 have also been filed or 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 USPTO to determine priority of invention, which could result in substantial cost to us, even if the eventual outcome is 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. See Item 3. "Legal Proceedings."

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. These conflicts, whether actual or perceived, 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, 2012, our research and development staff numbered 22 people, of whom four have Ph.Ds. Our research and development expenses for the years ended December 31, 2012, 2011 and 2010 were as follows:

Research and Development Cost by Program
(in millions)

Program	2012	2011	2010
AzaSite Plus/DexaSite	$ 6.6	$1.6	$0.1
BromSite	2.7	1.0	1.3
New products and other	0.4	0.7	0.7
Programs—non-specific	5.8	4.0	2.9
Total	$15.5	$7.3	$5.0

In 2012, program expenses included our AzaSite Plus/DexaSite program primarily related to costs for our Phase 3 clinical trial. We completed patient enrollment for the clinical trial in 2012 and enrolled more than 900 patients. Our BromSite program expenses primarily related to the costs of the Phase 3 clinical trial. We completed patient enrollment in 2012 and enrolled more than 240 patients. Non-specific program costs, which comprised facility, internal personnel and stock-based compensation costs that are not allocated to a specific development program, increased primarily due to an increase in headcount as a direct result of the Phase 3 clinical trial for AzaSite Plus/DexaSite and the Phase 3 clinical trial for BromSite. In addition, we continue to incur R&D expense to develop new product candidates.

In 2011, program expenses primarily consisted of non-specific program costs which comprised facility, internal personnel and stock-based compensation costs that are not allocated to a specific development program. Our AzaSite Plus/DexaSite program expenses primarily related to costs for a new Phase 3 clinical trial that we initiated in the fourth quarter of 2011. Our BromSite program expenses primarily related to the Phase 1/2 clinical trial that concluded in the first quarter of 2011 and the Phase 2 PK Study performed in the third quarter of 2011.

In 2010, program expenses primarily consisted of non-specific program costs which comprised facility, internal personnel and stock-based compensation costs that are not allocated to a specific development program. The decrease in non-specific costs in 2010 as compared to 2009 was primarily due to savings resulting from the Company's corporate restructuring in March 2009. Our BromSite program expenses primarily related to preclinical experiments and the Phase 1/2 clinical trial that was initiated in August 2010. Other program activities consisted primarily of new product development.

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 harmed.

Under the Merck License, Merck is responsible for the manufacture of AzaSite for the United States and Canada. The AzaSite NDA was transferred to Merck and manufacturing responsibilities for AzaSite were transferred to Merck for sales in the United States and Canada. We have a relationship with Catalent for the manufacture of AzaSite for sales outside the U.S. and Canada and for research and development purposes, as well as for other product candidates 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 our limited resources needed for the development of our product candidates. We do not currently plan on establishing a dedicated sales force or a marketing organization for our AzaSite, AzaSite Plus or other product candidates.

We have entered into corporate collaborations, and we may continue to pursue additional collaborations with one or more additional pharmaceutical companies in the United States and abroad, to market our products.

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. Many 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 comprised of a number of large and well-established companies, including Novartis/Alcon Laboratories, Inc., Allergan, Inc., Bausch & Lomb, Johnson & Johnson, Merck, 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 and 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.

Competition in our industry depends on a variety of factors including the ability to develop enhanced and innovative products, maintain a proprietary technology position, obtain required government approvals for products on a timely basis, attract and retain key personnel, effective and timely marketing of approved products and enter into effective collaborations for the manufacture, commercial marketing and distribution of 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 thereunder 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 testing;
- 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 (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 clinical 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. In 2011, we established the Scientific Advisory Board (SAB) to help guide and shape our research programs in the development of novel ophthalmic medicines. Members of the SAB represent leaders in ophthalmic research, treatment and clinical drug development, including Golman Peyman, M.D., Richard Lindstrom, M.D., Gary Foulks, M.D., Michael Lemp, M.D., and Kelly Nichols, O.D., M.P.H., Ph.D. The SAB is led by our Chief Medical Officer, Kamran Hosseini, M.D., Ph.D., and Brian Levy, O.D. M.Sc., a member of our Board of Directors, will also participate in all SAB meetings. Our SAB members possess deep insight into the etiology of important ocular diseases, which will be instrumental in advancing our therapeutic programs. Our SAB members have already made significant contributions to our current clinical development programs, providing input on trial protocols and endpoint design.

We plan to add additional 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.

Executive Officers of the Company

As of March 26, 2013, our executive officers were as follows:

Name	Title	Age
Timothy Ruane	Chief Executive Officer and member of the Board	48
Louis Drapeau	Vice President and Chief Financial Officer	69
Lyle M. Bowman, Ph.D.	Vice President, Development	64
Kamran Hosseini, M.D., Ph.D.	Vice President, Clinical & Regulatory Affairs and Chief Medical Officer	48
Surendra Patel	Vice President, Operations & Quality	57

Timothy Ruane joined us on December 1, 2010 as Chief Executive Officer and was elected as a member of the Board. Previously, Mr. Ruane served as President and Chief Executive Officer of Tekmira Pharmaceuticals and INEX Pharmaceuticals (which spun-out to Tekmira in 2007), a biopharmaceutical company, from 2005 to 2008. From 2004 to 2005, he served as the Senior Vice President of Corporate Development of INEX. From 2002 to 2004, Mr. Ruane was the Senior Vice President of Business Management of ILEX Oncology. Mr. Ruane has more than 24 years of experience with pharmaceutical and biotechnology companies in various management positions. Mr. Ruane has a Bachelor of Science degree in business finance from Wake Forest University and a Masters in Business Administration from the University of Washington.

Louis Drapeau joined us on October 1, 2007 as Vice President and Chief Financial Officer and served as the interim Chief Executive Officer from October 2008 through November 2010. 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, including 12 years as Managing Partner. He holds an undergraduate degree in mechanical engineering and a 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, he 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.

Kamran Hosseini joined us in February 2008 as Vice President, Clinical & Regulatory 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 director of ophthalmology drug delivery programs 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 & Quality. 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.

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

Employees

As of December 31, 2012, we had 30 employees, 27 of whom were full time. None of our employees are 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

Risks Relating to Our Business

It is difficult to evaluate our business because we are in an early stage of commercializing our products, our product candidates are still in clinical trials and successful development of pharmaceutical products is highly uncertain and requires significant expenditures, risk and time

We are still in an early stage of commercializing our products. AzaSite received regulatory approval in the U.S. in April 2007 and commercial sales of AzaSite began in the third quarter of 2007. Besivance received regulatory approval in May 2009 and commercial sales of Besivance began in the second half of 2009. 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 New Drug Applications, or NDAs. Successful development of pharmaceutical products is highly uncertain. Products that appear promising in research or development, 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. or international regulatory approvals or a delay in receiving such approvals due to, among other things, slow enrollment in clinical studies, failure to achieve study endpoints within the time period prescribed by the study, or at all, additional time requirements for data analysis or BLA or NDA preparation, discussions with the FDA, FDA requests for additional preclinical or clinical data, analyses or changes to study design; or 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 necessary manufacturing approvals;
- 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
- inability to compete with superior, equivalent, more cost-effective or more effectively promoted products offered by competitors.

Therefore, our research and development activities 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 failed to achieve clinical end points or 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 experienced declining sales in the United States and has not been commercially launched outside the United States.

Clinical trials are expensive, time-consuming and difficult to design, enroll and implement and there can never be any assurance that the results of such clinical trials will be favorable

Human clinical trials for our product candidates are very expensive and difficult to design, enroll and implement, in part because they are subject to rigorous regulatory requirements. A significant portion of our operating expenses in the year ended December 31, 2012 was incurred on our AzaSite Plus/DexaSite Phase 3 clinical trial and BromSite Phase 3 clinical trial. There can be no assurance that our AzaSite Plus/DexaSite Phase 3 clinical trial will meet its clinical endpoints as required by the FDA. The clinical trial process is also time-consuming. We may experience difficulties or delays in enrolling our clinical trials, which can delay the trials and our ability to obtain ultimate approval of our product candidates. In addition, we require various clinical materials to conduct our clinical trials and any unavailability or delay in our ability to obtain these materials may delay our trials, cause them to be more expensive or preclude us from completing these trials, which would harm our ability to obtain approval for our product candidates and therefore harm our business. We estimate that any particular clinical trial may take over a year to complete and will be very expensive. 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, among others:

- unforeseen safety issues;
- lack of effectiveness during clinical trials, including failure to meet required clinical endpoints;
- difficulty in determining dosing and trial protocols;
- slower than expected rates of patient recruitment;
- difficulties in obtaining clinical materials or participants necessary for the conduct of our clinical trials;
- 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 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, meet our expectations or defined clinical endpoints, or satisfy the FDA or other regulatory bodies. 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.

For example, results from our 2008 Phase 3 clinical trial of AzaSite Plus for the treatment of blepharoconjunctivitis showed improved clinical outcomes as compared to treatment with a corticosteroid or antibiotic alone in the reduction of inflammatory signs and symptoms and bacterial eradication, respectively. In addition, AzaSite Plus was very well tolerated. However, the trial did not achieve its primary clinical endpoint as defined by the protocol. We discussed the results of this trial with the FDA and determined a development plan

for AzaSite Plus. We cannot assure you that our current Phase 3 clinical trial for AzaSite Plus and DexaSite for blepharitis, or any future Phase 3 clinical trial for BromSite, will meet the prescribed clinical endpoints as defined in the protocol for these studies or that we will ever achieve FDA approval for the commercialization of AzaSite Plus, DexaSite, or BromSite.

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

We generally intend to enter into partnering and collaborative arrangements with respect to the commercialization of our product candidates, such as AzaSite Plus, DexaSite and BromSite. 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, among others:

- 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 further developing or 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 enter into 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. If we pursue a partnership for AzaSite Plus, DexaSite, BromSite or our other product candidates prior to successfully completing Phase 3 trials, we will likely receive less favorable economic terms than if we successfully completed Phase 3 trials.

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 and success of these third parties, particularly our partner Merck. Since Merck's acquisition of Inspire, the monthly prescriptions and our earned royalty revenues on net sales of AzaSite by Merck have decreased significantly. There can be no assurance that our royalty revenues from net sales of AzaSite will return to prior levels or will grow as originally anticipated. Our partners, including Merck, may terminate their relationships with us and/or may not diligently or successfully market or sell our products. These partners may also emphasize sales and marketing of their other products or 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 use 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, including Merck. If we are not successful in entering into future collaborations or maintaining our existing collaborations, particularly with Merck, we may be required to find new corporate collaborators or establish our own sales and marketing organization. We do not have a long-standing relationship with Merck and have limited information with respect to AzaSite and its marketing. The number of monthly prescriptions and sales of AzaSite have significantly declined since Merck took over marketing and sales of AzaSite after its acquisition of Inspire. While the minimum royalty payments from Merck have made up for this decline, there can be no assurance that

Merck will devote significant resources to, or successfully market and sell, AzaSite. There can be no assurance that we will ever receive higher, or equivalent, royalty revenues from Merck than we did from Inspire as an independent company. In addition, under the terms of the Merck License, Merck's obligation to make minimum royalty payments terminates in September 2013 and also may be suspended upon the occurrence of certain events, such as a requirement by the FDA or other governmental agency to suspend the marketing of AzaSite or withdraw it from the market in the United States or if we are unable to obtain commercial quantities of AzaSite for Merck to market and sell. Furthermore, Merck may terminate the Merck License at any time. If Merck were to terminate the Merck License, we would have to find a new marketing partner or market AzaSite ourselves. There can be no assurance that any new partnership would be possible or on similar terms as the Merck License or that it would be successful. We have no experience in sales, marketing or distribution and establishing such an organization would be costly. Moreover, there is no guarantee that a sales and marketing organization established by us would be successful. If we are unable to maintain existing collaborations, 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 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 that are conducting our clinical trials, including our current Phase 3 clinical trial for AzaSite Plus and DexaSite and our recently completed BromSite Phase 3 clinical trial, are not our employees and we anticipate that any future clinical trials of AzaSite Plus, DexaSite or BromSite will also be conducted by third parties. 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 United States and abroad. Any failure by those parties to perform their duties effectively, in compliance with clinical trial protocols, or on a timely basis, could delay or cause cancellation of our clinical trials, cause us to have to repeat the clinical trials, thereby increasing our expenses, harm our ability to develop and commercialize new products, harm our business and subject us to potential liabilities.

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, among others;
- effectiveness of marketing and distribution efforts by us and our licensees and distributors;
- cost-effectiveness of our products relative to competing products or treatments;
- actual or perceived benefits of competing products or treatments;
- physicians' comfort level and prior experience with and use of competing products or treatments; and
- availability of reimbursement for our products from government or other healthcare payers.

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. 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 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 for the sale by Merck of AzaSite in the United States and Canada, we will be required to pay for such additional licenses from our existing cash under the terms of the $60 million in aggregate principal amount of non-convertible, non-recourse promissory notes due in 2019 (AzaSite Notes).

In addition, 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.

A patent interference was declared before the Board of Patent Appeals and Interferences on certain U.S. patents covering AzaSite. Regents (Regents) of the University of California (University) assert that the

inventions contained in these patents were made by a former employee of the University alone, and without collaboration with us. They are asserting that they own those inventions, and that they are entitled to an award of priority of invention and a judgment that the inventions are not patentable to us. On November 25, 2011, the USPTO entered judgment against the University. On December 23, 2011, the University filed a Notice of Appeal to the Court of Appeals for the Federal Circuit in Washington, D.C., and on January 4, 2012, we filed a Notice of Cross-Appeal. We continue to believe the University's assertions are without merit and intend to vigorously contest those assertions. Oral arguments took place in November 2012 and no decision has yet been rendered. An adverse outcome of this interference could impact our royalty stream from Merck for AzaSite.

We received a letter (Notice Letter) dated April 15, 2011 from Sandoz, Inc. (Sandoz) providing notice that Sandoz has filed an Abbreviated New Drug Application (ANDA) with the FDA seeking marketing approval for a 1% azithromycin ophthalmic solution (Sandoz Product) prior to the expiration of the five U.S. patents listed in the Orange Books for AzaSite which include four of our patents and one patent licensed to us by Pfizer. In the paragraph IV Certification accompanying the Sandoz ANDA filing, Sandoz alleges that the claims of the Orange Book listed patents are invalid, unenforceable and/or will not be infringed by the Sandoz Product. On May 26, 2011, we, Merck and Pfizer filed a patent infringement lawsuit against Sandoz and related entities. The plaintiff companies have agreed that Merck will take the lead in prosecuting this lawsuit. Merck, with the assistance of Pfizer and us, will vigorously defend the five U.S. patents related to AzaSite. We own four U.S. patents covering AzaSite and its use, and have an exclusive license to a Pfizer-owned azithromycin patent. The filing of this lawsuit triggered an automatic stay, or bar, of the FDA's approval of the ANDA for up to 30 months or until a final district court decision of the infringement lawsuit, whichever comes first. We believe that our four patents and the Pfizer patent were properly prosecuted with the USPTO and are valid, and that three of these patents will provide AzaSite with exclusivity until March 2019. We and the other plaintiffs intend to vigorously enforce our patent rights relating to AzaSite and vigorously contest any Sandoz assertions that these patents are invalid or unenforceable. An adverse decision on the issues of validity or enforceability would significantly harm our royalty revenue stream from AzaSite.

Furthermore, the patents of others may impair our ability to commercialize our products. The patent positions of firms in the pharmaceutical and biotechnology 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 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, we would have to make payments on the AzaSite Notes out of our own cash resources, 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 and lose 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 (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 7 of the Consolidated Financial Statements in this Annual Report on Form 10-K for a more complete description of the terms of the AzaSite Notes.

Merck'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 Merck under the Merck License. Merck has full control of all promotional, sales and marketing activities for AzaSite in these territories, and has sole control over the pricing of AzaSite. The monthly prescriptions and our earned royalties on net sales of AzaSite have declined since Merck took over marketing and sales of AzaSite after its acquisition of Inspire. While the minimum royalty payments from Merck have made up for this decline, such payments terminate in September 2013 and there can be no assurance that Merck will devote significant resources to, or successfully market and sell, AzaSite. Accordingly, royalty payments in respect of net sales of AzaSite in the United States and Canada, if Merck markets AzaSite in Canada, are entirely dependent on the actions, efforts and success of Merck, over whom neither we nor our subsidiary have control. The success of Merck's commercialization of AzaSite and the timely repayment of the AzaSite Notes will depend on a number of factors, including, among others:

- the scope of Merck's marketing of AzaSite in the United States and, if launched, in Canada;
- Merck's commitment to continuing the Merck License with us;
- the effectiveness and extent of Merck's promotional, sales and marketing efforts;
- Merck's ability to successfully market AzaSite to physicians and patients;
- Merck's deployment of resources to market and sell AzaSite;
- Merck's ability to build, train and retain an effective sales force;
- Merck's marketing efforts outside of ophthalmologists;
- Merck's pricing decisions regarding AzaSite;
- Merck's marketing and selling of any current or future competing products;
- Merck's ability to compete against 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;
- the extent to which 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.

Merck may determine to focus its resources on its other products, internal development and other activities, which may harm its successful marketing of AzaSite and therefore impact our royalty payments.

Inspire historically promoted AzaSite to ophthalmologists. Pediatricians and primary care physicians write more than 67% of prescriptions for ophthalmic antibiotics. However, Inspire had no experience calling on pediatricians and primary care physicians. To date, Merck has continued to market AzaSite exclusively to ophthalmologists. There can be no assurance that Merck will more broadly market AzaSite. Inspire's and Merck's focus on eye care professionals rather than pediatricians and primary care providers may have resulted and, if continued, may continue to result in lower AzaSite sales and therefore lower royalties paid to us. A large number of pharmaceutical companies, including those with competing products and those with products for indications that are completely unrelated to AzaSite, compete for the time and attention of eye care professionals, pediatricians and primary care physicians. Neither we nor our subsidiary have any control over how Merck manages and operates its sales force, how effective Merck's sales efforts will be or Merck's pricing decisions regarding AzaSite.

In addition, Merck 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 Merck to incur higher product distribution costs, which would result in lower net sales of AzaSite.

Merck could deemphasize, sell, terminate or sublicense its rights to AzaSite. Neither we nor our subsidiary can prevent Merck 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 will be materially harmed to the extent Merck is unable or unwilling to successfully market and sell AzaSite. To the extent that our subsidiary fails to meet its payment obligations, we may make such payments out of our own cash resources in order to avoid a default under the AzaSite Notes, which we have done in the past. Failure to pay the interest due on two consecutive payment dates would constitute an event of default under the indenture, giving the right, but not the obligation, to noteholders to exercise their contractual remedies pursuant to the indenture. To the extent that an event of default occurs, the bondholders could seek available remedies, including foreclosure on our subsidiary. 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, we may not receive future revenue from AzaSite in North America.

Royalties under the Merck License may not be sufficient for our subsidiary to meet its payment obligations under the AzaSite Notes

Merck's obligation to pay royalties on net sales of AzaSite under the Merck License expires on a country-by-country basis upon the later of 11 years from the first commercial sale of AzaSite or when the last valid claim under one of our licensed patents covering a subject product under the Merck License in the United States and Canada expires. In the United States, first commercial sales occurred in August 2007, therefore, the obligation to pay royalties expires in August 2018. While our subsidiary will be entitled to minimum royalties under the Merck License through September 2013, 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 Merck's successful sales and marketing efforts for AzaSite in order for it to receive royalties in excess of these minimum amounts. In addition, under the terms of the Merck License, Merck's obligation to make minimum royalty payments may be suspended upon the occurrence of certain events, such as a requirement by the FDA or other governmental agency to suspend the marketing of AzaSite or withdraw it from the market in the United States or if we are unable to obtain commercial quantities of AzaSite for Merck to market and sell. Merck also has the right to terminate the Merck License at any time, in which case we would not receive any future royalties, including minimum royalties, from Merck. To the extent that royalties, including minimum royalties, are insufficient for our subsidiary to meet its payment obligations, we may make such payments out of our own cash resources in order to avoid a default under the notes, which we have done in the past. In addition, Merck'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 Merck licensed product to be withdrawn from the market or the marketing thereof

otherwise to be suspended in the United States or (ii) Merck is unable, despite use of commercially reasonable efforts, to obtain supply of any Merck licensed product in finished form in commercially reasonable amounts necessary to launch or market such Merck licensed product in the United States.

Royalties under the Merck License 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 Merck 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 Merck License, 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 Merck License 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 (Residual License Agreement). Under the terms of the Residual License Agreement, if the Merck License 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 an interim sublicense (Interim Sublicense), which is a part of the Residual License Agreement, 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. Merck can terminate the Merck License unilaterally in a variety of circumstances, including at any time in its discretion. If the Merck License 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 would have to 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 may not be successful and could harm our financial condition and results of operation. We may not be able to find a new third-party collaborator within the time period allowed and there can be no assurance that any such collaboration will be on acceptable terms or will be successful.

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 Merck License 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 Merck License shall remain with our subsidiary (whether or not the Merck License 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, as well as AzaSite Plus and AzaSite Xtra. 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 or Merck, 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, Merck'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 force us to make such payments out of our own cash resources in order to avoid a default under the AzaSite Notes and prevent or delay our ability to receive future revenue from AzaSite. Additional suppliers for azithromycin exist, but qualification of an alternative source would be required and could be time consuming and expensive and, during such qualification process, any shortage of azithromycin would negatively impact the sales of AzaSite and could delay the development timeline of AzaSite Plus and AzaSite Xtra.

In addition, certain of the raw materials that we use in formulating DuraSite, the drug delivery system used in AzaSite and our other products, 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 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 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.

We have to attract and retain key employees to be successful

A critical factor to our success will be retaining our personnel or recruiting replacement personnel. Competition for skilled individuals in the biotechnology business, particularly in the San Francisco Bay Area, is highly competitive, 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 we face. The loss of key personnel, the failure to recruit replacement personnel or to develop needed expertise would harm our business.

We may need to raise additional funds in the future, which could be difficult to obtain or could dilute the value and rights of our common stock, and if not obtained in satisfactory amounts, may prevent us from developing our products, conducting clinical trials or otherwise taking advantage of future opportunities or growing our business, any of which could harm our business

We may need to raise additional funds through equity, public or private debt, sale of assets or other arrangements, and we cannot be certain that we will be able to obtain additional financing on favorable terms, if at all. The current worldwide financing environment is challenging, particularly for smaller capitalized businesses such as ours, which could make it more difficult for us to raise funds on reasonable terms, or at all. If we issue additional equity securities, our stockholders will experience dilution and the new equity securities may have rights, preferences or privileges senior to those of existing holders of common stock. If we raise funds through debt, we will have to pay interest and may be subject to restrictive covenants, which would restrict operating flexibility and could harm our business. If we cannot raise sufficient funds on acceptable terms, if and when needed, we may not be able to develop our products, conduct clinical trials, have the financial strength and leverage to negotiate favorable terms with potential marketing partners, market our products, take advantage of future opportunities, grow our business or respond to competitive pressures or unanticipated industry changes, any of which could harm our business.

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 may be complementary or otherwise beneficial to us. Any of these acquisitions, if completed, could harm 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, among others:

- assimilating employees, operations, technologies and products from the acquired companies with our existing employees, operations, technologies and products;
- the potential need for additional funding to support our combined business;

- 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.

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 clinical trials 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. Therefore, we rely on a single contract manufacturer for a substantial portion of our manufacturing requirements. Any delays or difficulties that we may encounter in establishing and maintaining a relationship with qualified manufacturers to produce, package and distribute our products may harm our clinical trials, regulatory filings, market introduction and subsequent sales of our products.

Contract manufacturers must adhere to cGMP regulations that are strictly enforced by the FDA on an ongoing basis through the FDA's facilities inspection program, as well as by foreign governmental associations

outside the United States. Contract manufacturing facilities must pass a pre-approval plant inspection before the FDA will approve an 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 or could rescind their approval of the AzaSite manufacturing process or facility. Our dependence on third parties to manufacture our products may harm our ability to develop and deliver products on a timely and competitive basis. To the extent that we change manufacturers or engage additional manufacturers in the United States or abroad, we may experience delays, increased costs, quality-control issues and other issues that could harm our ability to conduct clinical trials and market and sell our products. Should we be required to manufacture products ourselves, we will:

- be required to expend significant amounts of capital to install a manufacturing capability;
- be subject to the regulatory requirements described above;
- be subject to similar risks regarding delays or difficulties encountered in manufacturing any such products; and
- 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.

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 healthcare 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, which could lead to lower reimbursement rates for our products or no reimbursement at all. 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 or our partners 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 the sale of these 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 may not be adequate to cover all potential claims we may encounter, particularly if AzaSite is commercialized outside the United States and Canada. If 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 2012, 2011, or 2010, 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.

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

As of December 31, 2012, our management and principal stockholders (those owning more than 5% of our outstanding shares) together beneficially owned approximately 52% of our shares of common stock. As a result, our management and principal stockholders, acting together or individually, 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, the approval of amendments to our charter, and the approval of business combinations and certain financing transactions. In September 2008, a group of our stockholders 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, future sales of equity or debt securities by us, the exercise of outstanding options and warrants that could result in dilution to our current holders of common stock, developments in our patents or other proprietary rights or those of our competitors, our own or Merck'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, 2012, our closing stock price fluctuated from a high of $0.50 to a low of $0.27. Such fluctuations can lead to securities class action litigation and make it difficult to obtain financing. 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 trades on the OTCBB

Our common stock currently trades on the over-the-counter bulletin board (OTCBB) market, although there are no assurances that it will continue to trade on this market. Over-the-counter (OTC) transactions involve risks in addition to those associated with transactions on a stock exchange. Listing on the OTC rather than a stock exchange could 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. Listing on the OTC could also cause a reduction in the number of investors willing or able 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 reduced. These factors could result in lower prices and larger spreads in the bid and ask prices for shares of common stock. Listing on the OTC could

also make our common stock substantially less attractive as collateral for loans, for investment by potential financing sources under their internal policies or state and federal securities laws or as consideration in future capital raising transactions. Furthermore, the listing on the OTC rather than a stock exchange may have other negative implications, including the potential loss of confidence by suppliers, partners and employees. Our OTC status may also make it more difficult and expensive for us to comply with state and federal securities laws in connection with future financings, acquisitions or equity issuances to employees and other service providers, thereby making it more difficult and expensive for us to raise capital, acquire other businesses using our stock and compensate our employees using equity.

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 our preferred stock (Preferred Stock). Our Board of Directors has the authority to determine the price, rights, preferences, privileges and restrictions, including voting rights, of the 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 harmed 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 that 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 use the equipment at our contract manufacturing site we could conduct our pilot plant operations although we would incur significant additional costs and delays in our product development timelines.

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, including the recent downgrade by Standard & Poor's of the U.S. debt rating, could negatively affect our ability to liquidate 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 and our $22.2 million financing in July 2011, investment income has become a more substantial component of our 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 income.

We are subject to risks related to our information technology systems and the information gathered in our clinical trials

We rely on information technology systems in order to conduct business, including internal and external communications, ordering materials for our operations, storing operational information and maintaining and reporting our results. These systems are vulnerable to interruption or failure due to the age of certain of our systems, viruses, malware, security breaches, fire, power loss, system malfunction and other events, which may be beyond our control. Systems interruptions or failures could reduce our ability to develop our products or continue our business, which could have a material adverse effect on our operations and financial performance.

Additionally, federal and state laws governing our ability to obtain and, in some cases, to use and disclose data we need to conduct research activities, including our clinical trials, could increase our costs of doing business. These laws' requirements could further complicate our ability to obtain necessary research data from our collaborators. In the event that our systems are breached and certain clinical data is compromised, we could become subject to costs arising from failure to maintain the privacy of protected health information. Claims that we have violated individuals' privacy rights or breached our privacy obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

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. In October 2010, we subleased approximately 11,640 square feet of office space at this facility. The sublease expires on December 31, 2013. We believe our existing facilities will be suitable and adequate to meet our needs for the immediate future.

Item 3. Legal Proceedings

We are subject to various claims and legal actions during the ordinary course of our business. On November 30, 2009, a patent interference was declared before the Board of Patent Appeals and Interferences on certain U.S. patents covering AzaSite. Regents of the University assert that the inventions contained in these patents were made by a former employee of the University alone, and without collaboration with us. They are asserting that they own those inventions, and that they are entitled to an award of priority of invention and a judgment that the inventions are not patentable to us. On November 25, 2011, the USPTO entered judgment against the University. On December 23, 2011, the University filed a Notice of Appeal to the Court of Appeals for the Federal Circuit in Washington, D.C., and on January 4, 2012, we filed a Notice of Cross-Appeal. Oral arguments took place in November 2012 and no decision has yet been rendered. We continue to believe the University's assertions are without merit and we will continue to vigorously defend our position.

We received a Notice Letter stating that Sandoz has filed an ANDA with the FDA seeking marketing approval for the Sandoz Product prior to the expiration of the five US patents listed in the Orange Books for AzaSite, which include four of our patents and one patent licensed to us by Pfizer. In the paragraph IV Certification accompanying the Sandoz ANDA filing, Sandoz alleges that the claims of the Orange Book listed patents are invalid, unenforceable and/or will not be infringed by the Sandoz Product. On May 26, 2011, we, Merck and Pfizer filed a patent infringement lawsuit against Sandoz and related entities. The plaintiff companies have agreed that Merck will take the lead in prosecuting this lawsuit. The filing of this lawsuit triggered an automatic stay, or bar, of the FDA's approval of the ANDA for up to 30 months or until a final district court decision of the infringement lawsuit, whichever comes first. We and the other plaintiffs intend to vigorously enforce our patent rights relating to AzaSite and vigorously contest any Sandoz assertions that these patents are invalid or unenforceable.

On January 3, 2013, Janel Joseph and Mitchell Joseph III filed a complaint in circuit court in Fayette County, Kentucky against Bausch & Lomb and us alleging that Janel Joseph was injured when her physician treated her with the Bausch & Lomb product Besivance following a photorefractive keratectomy. The plaintiffs allege that the use was off-label but nonetheless marketed by the defendants. Ms. Joseph alleges loss of vision and Mr. Joseph, her husband, alleges loss of consortium. On February 1, 2013, Bausch & Lomb removed the case to the United States District Court for the Eastern District of Kentucky. On February 8. 2013, the defendants filed answers denying the allegations. There have been no further proceedings. The plaintiffs to date have not made a specific claim for damages.

We believe that there are currently no other claims or legal actions that would have a material adverse impact on our financial position, operations or potential performance.

Item 4. Mine Safety Procedures.

Not applicable.

PART II

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

Market Information

Since April 21, 2009, our common stock has traded on the OTCBB market under the symbol "INSV." OTC market quotations reflect inter-dealer prices, without retail mark-up, mark-down or commission and may not necessarily represent actual transactions. From September 30, 2008 to April 20, 2009, our common stock 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 closing sales prices for our common stock as reported by the OTCBB for the periods indicated. These prices do not include retail mark-ups, mark-downs or commissions.

2012	High	Low
First Quarter	0.50	0.36
Second Quarter	0.41	0.27
Third Quarter	0.46	0.32
Fourth Quarter	0.39	0.29

2011	High	Low
First Quarter	0.60	0.30
Second Quarter	0.93	0.63
Third Quarter	0.70	0.48
Fourth Quarter	0.54	0.38

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

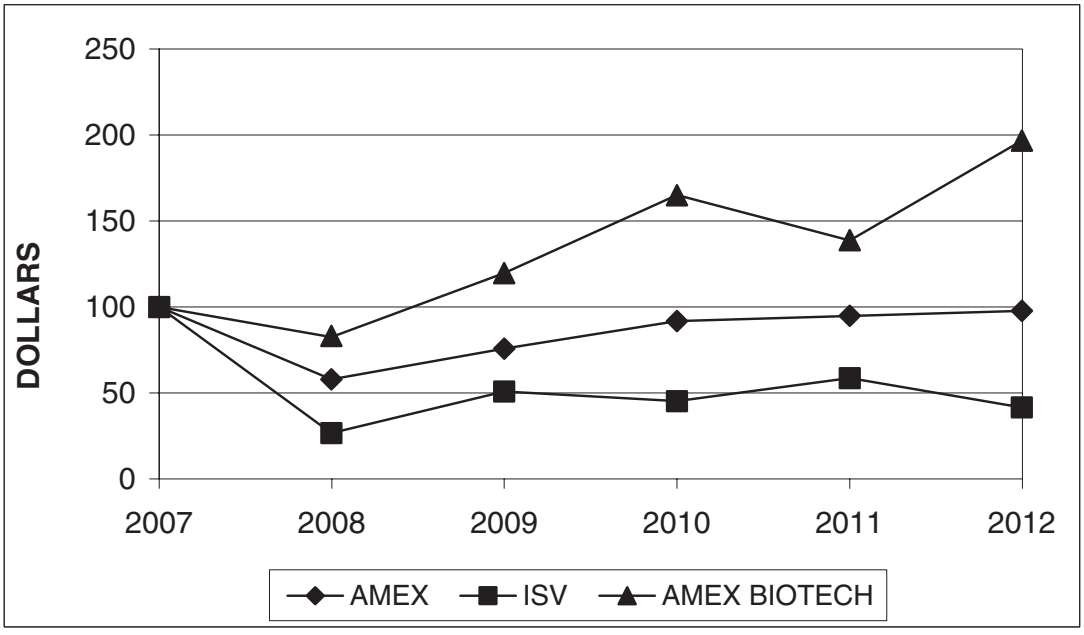
Information regarding employee stock-based compensation is provided in Note 11 in the Notes to the Consolidated Financial Statements in Item 8 of Part II of this Annual Report on Form 10-K.

As of March 19, 2013, we had approximately 164 registered stockholders of record of our Common Stock. On March 19, 2013, the last sale price reported on the OTCBB for our common stock was $0.34 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, 2007 through December 31, 2012 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, 2007 in each of the foregoing indices and (ii) reinvestment of dividends, if 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.



	AMEX	ISV	AMEX BIOTECH
12/31/07	100	100	100
12/31/08	58	27	82
12/31/09	76	51	120
12/31/10	92	45	165
12/31/11	95	59	139
12/31/12	98	41	197

Notwithstanding anything to the contrary set forth in any of our previous filings under the Securities Act or the Securities Exchange Act of 1934, as amended (Exchange Act) 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 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 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 financial data for us for the five years ended December 31, 2012 (in thousands except per share amounts):

	Year Ended December 31,				
(in thousands, except per share data)	**2012**	**2011**	**2010**	**2009**	**2008**
Statement of Operations Data					
Revenues:					
Royalties	$ 21,641	$ 15,138	$ 11,120	$ 8,000	$ 3,596
Licensing fee, milestone amortization and other	—	785	747	1,798	10,110
Total revenues	21,641	15,923	11,867	9,798	13,706
Expenses:					
Research and development	15,479	7,337	4,974	5,436	16,242
General and administrative	5,781	5,645	4,511	5,792	8,251
Cost of revenues, principally royalties to third parties	1,062	1,917	1,727	1,549	630
Severance	—	—	—	527	1,909
Impairment of property and equipment	—	—	—	615	—
Total expenses	22,322	14,899	11,212	13,919	27,032
Interest expense and other, net	(9,494)	(10,167)	(10,248)	(10,034)	(7,984)
Change in fair value of warrant liability	1,898	2,201	—	—	—
Net loss	$ (8,277)	$ (6,942)	$ (9,593)	$(14,155)	$(21,310)
Net loss per share:					
Loss per share—basic	$ (0.06)	$ (0.06)	$ (0.10)	$ (0.15)	$ (0.23)
Loss per share—diluted	$ (0.06)	$ (0.06)	$ (0.10)	$ (0.15)	$ (0.23)
Weighted average shares used in per share calculation:					
—Basic	131,951	111,769	94,774	94,710	94,607
—Diluted	131,951	111,769	94,774	94,710	94,607

	As of December 31,				
(in thousands)	**2012**	**2011**	**2010**	**2009**	**2008**
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 9,322	$ 26,395	$ 16,468	$ 24,721	$ 37,456
Working capital, exclusive of deferred revenues	(3,424)	14,303	14,104	22,816	35,068
Total assets	17,759	32,401	23,586	32,246	44,943
Non-recourse secured notes payable	51,883	58,558	60,000	60,000	60,000
Accumulated deficit	(207,804)	(199,527)	(192,585)	(182,992)	(168,837)
Total stockholders' equity (deficit)	$ (41,869)	$ (34,539)	$ (42,220)	$ (33,033)	$ (19,506)

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 Annual Report on Form 10-K.

Overview

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

Our DuraSite sustained drug delivery technology is a proven synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a drug as a solution, gel or suspension and can be customized for delivering a wide variety of drug candidates. We have focused our research and development and commercial support efforts on the following topical products formulated with our DuraSite drug delivery technology.

- AzaSite® (azithromycin ophthalmic solution) 1% is a DuraSite formulation of azithromycin, a broad spectrum ocular antibiotic approved by the U.S. Food and Drug Administration (FDA) in April 2007 to treat bacterial conjunctivitis (pink eye). It was commercialized in the United States by Inspire Pharmaceuticals, Inc. (Inspire) beginning in August 2007. The key advantages of AzaSite are a significantly reduced dosing regimen leading to better compliance and outcome, a trusted broad spectrum antibiotic, and a lowered probability of bacterial resistance based on high tissue concentration. In May 2011, Merck & Co. (Merck) acquired Inspire and Inspire became a wholly-owned subsidiary of Merck. Merck is now responsible for commercializing AzaSite in North America. We receive a 25% royalty on net sales of AzaSite in North America, plus minimum royalties if applicable.
- Besivance® (besifloxacin ophthalmic suspension) 0.6% is a DuraSite formulation of besifloxacin, a broad spectrum ocular antibiotic approved by the FDA in May 2009 to treat bacterial conjunctivitis (pink eye). An advantage of Besivance is a faster rate of resolution of the infection that may reduce the duration of the illness and reduce the chances of infecting others. Besivance was developed by Bausch + Lomb Incorporated (Bausch & Lomb) and launched in the United States in the second half of 2009. In 2011, Besivance was launched internationally in select countries. We receive a middle single-digit royalty on net sales of Besivance globally.
- AzaSite Plus™ (ISV-502) is a fixed combination of azithromycin and dexamethasone in DuraSite for the treatment of ocular inflammation and infection (blepharitis and/or blepharoconjunctivitis) for which there is no FDA approved indicated treatment. We completed a Phase 3 trial in November 2008 for the treatment of blepharoconjunctivitis and AzaSite Plus was very well tolerated. Although efficacious, the trial did not achieve its primary clinical endpoint as defined by the previous protocol. We discussed the results of this trial with the FDA and determined a new development plan for this product candidate. In May 2011, we reached an agreement with the FDA on a Special Protocol Assessment (SPA) for the design of a Phase 3 clinical trial of AzaSite Plus in patients with blepharitis. An SPA is a written agreement with the FDA that the study design and planned analysis of the sponsor's Phase 3 clinical trial adequately addresses the objectives necessary to support a regulatory submission. In November 2011, we initiated a new Phase 3 clinical trial for this product candidate in blepharitis and completed patient enrollment in the clinical trial in September 2012. This study enrolled more than 900 patients and we expect to receive top-line data in the second quarter of 2013.
- DexaSite™ (ISV-305) is a DuraSite formulation of dexamethasone in development for the treatment of ocular inflammation. DexaSite is included in the Phase 3 clinical trial SPA for AzaSite Plus. In November 2011, we initiated a Phase 3 clinical trial for this product candidate in blepharitis and completed patient enrollment in the clinical trial in September 2012. This study enrolled more than 900 patients and we expect to receive top-line data in the second quarter of 2013.

- BromSite™ (ISV-303) is a DuraSite formulation of bromfenac in development for the treatment of post-operative inflammation and eye pain. We initiated a Phase 1/2 clinical trial for this product candidate in August 2010 and we received positive top-line results from this study in the first quarter of 2011, which demonstrated the efficacy and safety of BromSite. In the third quarter of 2011, we completed an additional Phase 2 clinical trial to investigate the pharmacokinetics (PK) of BromSite in humans. We received positive top-line results that showed that the mean concentration of bromfenac in the aqueous humor of patients using BromSite was more than double compared to the currently available bromfenac eye product. In July 2012, we initiated a Phase 3 clinical trial for this product candidate and completed patient enrollment in November 2012 with 268 patients enrolled. In March 2013, we received positive top-line results that demonstrated a reduction of inflammation and pain after cataract surgery at a lower drug concentration compared to the current market leader.
- DuraSite 2® is our next-generation enhanced drug delivery system, which is designed to provide a broad platform for developing superior ophthalmic therapeutics. DuraSite 2 is based on the original DuraSite technology, and incorporates a cationic polymer to achieve sustained and enhanced ocular delivery of drugs. DuraSite 2 is designed to increase the tissue penetration for topically delivered ocular drugs with the aim of improved efficacy and dosing convenience. We obtained preclinical data from a comparative study that demonstrated superior drug retention and tissue penetration compared to DuraSite. We plan to utilize the DuraSite 2 platform in future pipeline product candidates and expect that it will be available for license for our other drugs. A patent application for DuraSite 2 was submitted to the U.S. Patent and Trademark Office (USPTO) in 2009.
- ISV-101 is a DuraSite formulation with a low concentration of bromfenac for the treatment of dry eye disease. We filed an Investigational New Drug Application (IND) with the FDA for this product candidate in the first quarter of 2011. We plan to initiate a Phase 1/2 clinical trial for this product candidate, but no time period has been set.

Major Developments

Our recent major developments and events include:

- In July 2012, we initiated the BromSite Phase 3 clinical trial. We completed patient enrollment in November 2012 with 268 patients enrolled and received positive top-line results in March 2013;
- In August 2012, we amended the payment terms of the existing Merck License. On a quarterly basis, Merck will pay us the higher of the pro-rata annual minimum royalty or the earned royalty for 2012 and 2013. In addition, in August 2012, Merck paid us a $7.3 million catch-up payment for the difference between the earned royalties already paid for the fourth quarter of 2011 and the first and second quarters of 2012, and the pro-rata annual minimum royalties for those quarters;
- In September 2012, we completed patient enrollment for the AzaSite Plus and DexaSite Phase 3 clinical trial and enrolled more than 900 patients. We expect to have top-line data in the second quarter first half of 2013; and
- In September 2012, we introduced DuraSite 2, our next-generation enhanced drug delivery system and announced preclinical data from a study that demonstrated superior drug retention and tissue penetration compared to DuraSite.

Business Strategy

Our business strategy consists of the following:

1. **Develop our pipeline of ocular product candidates.** We seek to identify new product candidates from proven drugs that can be improved by formulation in DuraSite, which can substantially reduce the clinical risk involved in these product candidates. As appropriate, we plan to conduct preclinical and clinical testing of our product candidates.

2. **Partner our product candidates.** When we deem it appropriate, we seek to partner with larger pharmaceutical companies to manufacture and market our products. Partnering agreements generally include upfront and milestone payments, as well as on-going royalty payments upon commercialization, payable to us.

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 when four basic criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured. We have arrangements with multiple revenue-generating elements. We analyze our multiple element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting. An item can generally be considered a separate unit of accounting if both of the following criteria are met: the delivered item(s) has value to the customer on a stand-alone basis and if the arrangement includes a general right of return and delivery or performance of the undelivered item(s) is considered probable and substantially in our control. Items that cannot be divided into separate units are combined with other units of accounting, as appropriate. Consideration received is allocated among the separate units based on the unit's estimated selling price and is recognized in full when the criteria are met. We deem service to be rendered if no continuing obligation exists on our part.

Our revenues are primarily related to royalties on product sales and licensing agreements, and such agreements may provide for various types of payments, including upfront payments, research funding and related fees during the terms of the agreements, milestone payments based on the achievement of established development objectives and licensing fees.

We receive 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 collectability is reasonably assured.

Revenue associated with non-refundable up-front license fees under arrangements where the license fees cannot be accounted for as separate units of accounting is deferred and recognized as revenue on a straight-line basis over the expected term of our continued involvement. Revenues from the achievement of milestones are recognized as revenue when the milestones are achieved and the milestone payments are due and collectible.

For the year ended December 31, 2011, we adopted amendments to the accounting standard related to multiple-deliverable revenue arrangements. The amendment requires entities to allocate revenue in multiple-deliverable revenue arrangements using estimated selling prices of the delivered goods and services based on a selling price hierarchy. The amendment eliminated the residual method of revenue allocation and requires revenue to be allocated using the relative selling price method. The adoption of this amendment did not impact our consolidated financial position or results of operations since we did not enter into or materially modify revenue arrangements during the years ended December 31, 2012 and 2011. In addition, there have been no significant changes to the units of accounting, the allocation of consideration received to the various units of accounting, and the timing of revenue recognition based on this amendment. We do not expect the adoption of this amendment to have a material impact on future periods.

Income Taxes. We account for income taxes under the liability method. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax reporting bases of

assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Realization of deferred tax assets is dependent upon future earnings, the timing and amount of which are uncertain. We record a valuation allowance against deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. When we establish or reduce the valuation allowance related to the deferred tax assets, our provision for income taxes will increase or decrease, respectively, in the period such determination is made.

We utilize a two-step approach to recognize and measure uncertain tax positions, if any. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained upon tax authority examination, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement.

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 (1994 Plan) and its successor the 2007 Performance Incentive Plan (2007 Plan). In addition, we have a qualified employee stock purchase plan (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. In August 2009, the Purchase Plan was suspended. The benefits provided by these plans qualify as stock-based compensation 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 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.

Our revenues for the years ended December 31, 2012, 2011 and 2010 were, as follows:

	Year Ended December 31,		
	2012	2011	2010
AzaSite royalties	$19.5	$13.9	$10.7
Besivance royalties	2.1	1.2	0.5
Other	—	0.8	0.7
Total	$21.6	$15.9	$11.9

For 2012, AzaSite royalties included $7.6 million of royalties based on net sales and an additional $11.9 million minimum royalty true-up payment by Merck. The increase in royalties was driven by an increase in the required minimum royalty to $17 million for the fiscal year ended September 30, 2012, the measurement period pursuant to the terms of the Merck License, and the pro-rata share of $19 million for the fiscal year ended September 30, 2013. Merck's obligation to make minimum royalty payments terminates in September 2013 and also may be suspended upon the occurrence of certain events, such as a requirement by the FDA or other governmental agency to suspend the marketing of AzaSite or withdraw it from the market in the United States. In addition, a decline in net sales of AzaSite by Merck further increased the minimum royalty true-up payment. Earned AzaSite royalties declined by 24% compared to the same period in 2011. The increase in Besivance royalties in 2012 was driven by an increase in net sales of Besivance by Bausch & Lomb.

For 2011, AzaSite royalties included $10.0 million of royalties based on net sales and an additional $3.9 million minimum royalty true-up payment by Merck. The increase in royalties was driven by an increase in the required minimum royalty to $15 million for the fiscal year ended September 30, 2011. In addition, a decline in net sales of AzaSite by Merck further increased the minimum royalty true-up payment. The increase was offset by a 6% decrease in AzaSite net sales. The increase in Besivance royalties was driven by an increase in net sales of Besivance. Revenues in 2011 also included $0.5 million from the sale of azithromycin to Merck and certain international partners under supply agreements and $0.3 million from the amortization and recognition of international license fee payments for AzaSite.

In 2010, revenues primarily consisted of $10.7 million of earned royalties from net sales of AzaSite by Merck. compared to $8.0 million in 2009. The $2.7 million increase in royalty revenues from the prior year was primarily due to a 22% increase of AzaSite net sales in the United States. In addition, the royalty rate for AzaSite increased from 20% to 25% in July 2009. 2010 revenues also included $0.5 million of royalties from net sales of Besivance by Bausch & Lomb, $0.5 million of grant income under the Therapeutic Discovery Program and $0.2 million from the sale of materials to Merck under the Supply Agreement.

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 2012, 2011 and 2010 (in thousands):

	Year Ended December 31,		
	2012	2011	2010
Research	$ 5,047	$4,468	$3,137
Clinical development	10,432	2,869	1,837
Total research and development	$15,479	$7,337	$4,974

Our research and development expenses by program for 2012, 2011 and 2010 (in millions) were:

Program	2012	2011	2010
AzaSite Plus/DexaSite	$ 6.6	$1.6	$0.1
BromSite	2.7	1.0	1.3
New products and other	0.4	0.7	0.7
Programs—non-specific	5.8	4.0	2.9
Total	$15.5	$7.3	$5.0

Research and development expenses were $15.5 million in 2012. In 2012, program expenses consisted of our AzaSite Plus/DexaSite program primarily related to costs for our Phase 3 clinical trial. We completed patient enrollment for the AzaSite Plus/DexaSite clinical trial in 2012 and enrolled more than 900 patients. Our BromSite program expenses primarily related to the costs for our Phase 3 clinical trial. We completed patient enrollment for the BromSite clinical trial in 2012 and enrolled more than 240 patients. Non-specific program costs, which comprised facility, internal personnel and stock-based compensation costs that are not allocated to a specific development program, increased primarily due to an increase in headcount as a direct result of the Phase 3 clinical trials. In addition, we continue to incur R&D expense to develop new product candidates.

Research and development expenses were $7.3 million in 2011. In 2011, program expenses primarily consisted of non-specific program costs which comprised facility, internal personnel and stock-based compensation costs that are not allocated to a specific development program. Our non-specific program costs increased in 2011 compared to 2010, primarily due to an increase in headcount. Our AzaSite Plus/DexaSite program expenses primarily related to costs for a new Phase 3 clinical trial that we initiated in the fourth quarter of 2011. Our BromSite program expenses primarily related to the Phase 1/2 clinical trial that concluded in the first quarter of 2011 and the Phase 2 PK Study performed in the third quarter of 2011.

Research and development expenses were $5.0 million in 2010. In 2010, our program expenses primarily consisted of non-specific program costs which comprised facility, internal personnel and stock-based compensation costs that are not allocated to a specific development program. The non-specific costs decreased in 2010 compared to 2009, primarily due to savings resulting from our corporate restructuring in March 2009. Our BromSite program expenses primarily related to preclinical experiments and the Phase 1/2 clinical trial that was initiated in August 2010.

Our future research and development expenses will depend on the results and magnitude or scope of our clinical, preclinical and research activities and requirements imposed by regulatory agencies. Accordingly, our research and development expenses may fluctuate significantly from period to period. In addition, if we in-license or out-license rights to product candidates, our research and development expenses may fluctuate significantly.

General and administrative.

General and administrative expenses increased to $5.8 million in 2012 from $5.6 million in 2011. In 2012, we incurred slightly higher costs related to financial reporting services and investor relations.

General and administrative expenses increased to $5.6 million in 2011 from $4.5 million in 2010. In 2011, we incurred higher personnel-related costs due to an increase in headcount and higher legal expenses pertaining to patent litigation with the Regents of the University and Sandoz.

Cost of revenues.

Our cost of revenues were $1.1 million, $1.9 million and $1.7 million for 2012, 2011 and 2010, respectively. Cost of revenues were primarily comprised of royalties accrued for third parties, including Pfizer, based on AzaSite net sales by Merck. In 2011 and 2010, cost of revenues also included the cost of the azithromycin supplied to Merck and international partners under supply agreements.

Interest expense and other, net.

Interest expense and other, net, was an expense of $9.5 million, $10.2 million and $10.2 million for 2012, 2011 and 2010, respectively. Interest expense was primarily due to the interest expense on the non-recourse AzaSite Notes issued in February 2008 and related amortization of the debt issuance costs incurred from our issuance of the AzaSite Notes. Interest expense decreased in 2012 as a result of pay downs of principal on the AzaSite Notes.

Change in fair value of warrant liability.

Change in fair value of warrant liability was income of $1.9 million and $2.2 million for 2012 and 2011, respectively. The income resulted from a decrease in the fair value of our warrant liability that was initially valued as of July 18, 2011 and revalued as of December 31, 2012 and 2011. The decrease in fair value was primarily driven by a decrease in our stock price.

Liquidity and Capital Resources

In recent years, we have financed our operations primarily through private placements of equity securities, debt financings and payments from corporate collaborations. At December 31, 2012 and 2011, our cash, cash equivalents and short-term investments were $9.3 million and $26.4 million, respectively. 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.

We have incurred significant losses since inception, including net losses of approximately $8.3 million, $6.9 million and $9.6 million for the years ended December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012, our accumulated deficit was $207.8 million.

We believe we have available funds to enable us to meet our obligations for approximately the next 12 months. Our ability to fund our operations is dependent primarily upon our ability to execute on our business plan, including generating sufficient cash inflows from operating activities and obtaining additional funding.

We will need to raise additional funding to support our operating activities. Adequate funding may not be available on acceptable terms, or at all. The failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition. The accompanying financial statements do not include any adjustments that might result from the outcome of these uncertainties.

Cash used in operating activities was $10.3 million, $8.9 million and $8.1 million for 2012, 2011 and 2010, respectively. The increase in 2012 compared to 2011 was primarily due to our Phase 3 clinical trials related to AzaSite Plus/DexaSite and BromSite. This cost increase was offset by an $11.9 million AzaSite minimum royalty true-up payment received from Merck. The increase in 2011 compared to 2010 was primarily due to higher personnel costs related to an increase in headcount and costs incurred to prepare for clinical trials related to AzaSite Plus, DexaSite, BromSite and ISV-101. This cost increase was offset by a $3.9 million AzaSite minimum royalty true-up payment received from Merck.

Cash provided by investing activities was $16.4 million and $12.4 million for 2012 and 2010, respectively. Cash used in investing activities was $19.7 million for 2011. In 2012 and 2010, we converted $16.5 million and $12.5 million, respectively, from short-term investments to cash and cash equivalents. In 2011, we invested $19.5 million in short-term investments.

Cash used in financing activities was $6.7 million for 2012. Cash provided by financing activities was $19.0 million and $16,000 for 2011 and 2010, respectively. In 2012 and 2011, we made principal payments of $6.7 million and $1.4 million, respectively, on the AzaSite Notes. In July 2011, we completed a private placement financing transaction in which we sold shares of common stock and warrants to purchase shares of common stock, which resulted in approximately $20.4 million in net proceeds to us after deducting placement agent fees, legal, accounting and other costs associated with the transaction. We intend to use the net proceeds of the transaction to fund clinical trials and for general corporate purposes, including working capital.

The tables below set forth the amount of cash that we raised for fiscal years 2010 through 2012 from equity financings and option exercises.

Cash Received from Private Placements of Equity Securities

Date	Net Proceeds	Shares of Common Stock Issued
July 2011	$20.4 million	37.0 million plus warrants to purchase 14.8 million shares

Cash received from Option Exercises

Year	Net Proceeds
2011	$ 58,000
2010	$ 21,000

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 any 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 2013. 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 materially harm 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, 2012 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
Purchase obligations(1)	$ 2,918	$ 2,918	$ —	$ —	$ —
Facilities lease obligations(2)	848	848	—	—	—
Licensing agreement obligations(3)	4,772	876	1,540	1,540	816
Secured notes payable(4)	51,883	10,395	—	—	41,488
Interest payments on secured notes payable(5)	42,553	7,704	13,276	13,276	8,297
Total commitments	$102,974	$22,741	$14,816	$14,816	$50,601

(1) Purchase obligations include commitments related to clinical development.
(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 royalty payments for the life of the licensed patents. The estimated royalties due under certain of these agreements are as noted for 2013 through 2019.
(4) Principal repayments are limited to royalties received from Merck from net 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 and future projected sales. The AzaSite Notes are due in 2019.
(5) Interest repayments represent an estimate based on expected principal repayments.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

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

We have debt in the form of non-recourse, secured notes payable with fixed interest rates. As a result, our exposure to market risk caused by fluctuations in interest rates is minimal. We had $51.9 million in the AzaSite Notes outstanding as of December 31, 2012, with a fixed interest rate of 16%. If the market interest rates were to increase by 10% from the December 31, 2012 levels, it would not result in an increase in interest expense. At December 31, 2012, our debt was reflected in the accompanying unaudited condensed consolidated financial statements at face value. Due to a decline in and uncertainty regarding AzaSite earned royalty revenues, it is reasonably possible that the fair value of the debt has declined. The decline in value of debt is not reasonably determinable at this time.

The securities in our investment portfolio are not leveraged and are subject to minimal interest rate risk. Due to their original maturities of twelve months or less, the securities are classified as cash and cash equivalents or short-term investments. They are classified as trading securities principally bought and held for the purpose of selling them in the near term, with unrealized gains and losses included in earnings. 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% from the December 31, 2012 levels would cause a decrease in interest income, it would not likely 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. To achieve this objective in the current economic environment, we maintain our portfolio in cash equivalents or short-term investments, including obligations of U.S. government-sponsored enterprises and money market funds. These securities are classified as cash and cash equivalents or short-term investments 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

The Board of Directors and Stockholders of
InSite Vision Incorporated

We have audited the accompanying consolidated balance sheets of InSite Vision Incorporated and subsidiaries (the "Company") as of December 31, 2012 and 2011, and the related consolidated statements of operations, stockholders' deficit, and cash flows for each of the three years in the period ended December 31, 2012. 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. 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, 2012 and 2011, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2012, in conformity with accounting principles generally accepted in the United States of America.

/s/ Burr Pilger Mayer, Inc.

San Francisco, California
March 26, 2013

INSITE VISION INCORPORATED

CONSOLIDATED BALANCE SHEETS

(in thousands, except share data)	December 31, 2012	December 31, 2011
ASSETS		
Current assets:		
Cash and cash equivalents	$ 1,323	$ 1,900
Short-term investments	7,999	24,495
Accounts receivable, net	5,250	2,564
Prepaid expenses and other current assets	144	12
Total current assets	14,716	28,971
Property and equipment, net	377	345
Debt issuance costs, net	2,666	3,085
Total assets	$ 17,759	$ 32,401
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 677	$ 703
Accrued liabilities	1,535	411
Accrued compensation and related expense	1,134	978
Accrued royalties	1,104	964
Accrued interest	1,038	1,171
Non-recourse secured notes payable, current	10,395	6,286
Warrant liability	2,257	4,155
Total current liabilities	18,140	14,668
Non-recourse secured notes payable, long-term	41,488	52,272
Total liabilities	59,628	66,940
Commitments and contingencies (Note 8)		
Stockholders' deficit:		
Preferred stock, $0.01 par value, 5,000,000 shares authorized, none issued and outstanding	—	—
Common stock, $0.01 par value, 240,000,000 shares authorized; 131,951,033 shares issued and outstanding at December 31, 2012 and 2011	1,320	1,320
Additional paid-in capital	164,615	163,668
Accumulated deficit	(207,804)	(199,527)
Total stockholders' deficit	(41,869)	(34,539)
Total liabilities and stockholders' deficit	$ 17,759	$ 32,401

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except per share data)	Year Ended December 31, 2012	2011	2010
Revenues:			
Royalties	$ 21,641	$ 15,138	$ 11,120
Licensing fee and milestone amortization	—	275	—
Other product and service revenues	—	510	747
Total revenues	21,641	15,923	11,867
Expenses:			
Research and development	15,479	7,337	4,974
General and administrative	5,781	5,645	4,511
Cost of revenues, principally royalties to third parties	1,062	1,917	1,727
Total expenses	22,322	14,899	11,212
Income (loss) from operations	(681)	1,024	655
Interest expense and other, net	(9,494)	(10,167)	(10,248)
Change in fair value of warrant liability	1,898	2,201	—
Net loss	$ (8,277)	$ (6,942)	$ (9,593)
Net loss per share:			
Loss per share—basic	$ (0.06)	$ (0.06)	$ (0.10)
Loss per share—diluted	$ (0.06)	$ (0.06)	$ (0.10)
Weighted average shares used in per share calculation:			
—Basic	131,951	111,769	94,774
—Diluted	131,951	111,769	94,774

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT

(in thousands, except share data)	Common Stock Shares	Common Stock Amount	Additional Paid-in-Capital	Accumulated Deficit	Total Stockholders' Deficit
Balances, December 31, 2009	94,738,400	$ 947	$149,012	$(182,992)	$(33,033)
Issuance of common stock from exercise of stock options	84,193	1	20	—	21
Stock-based compensation	—	—	385	—	385
Net loss	—	—	—	(9,593)	(9,593)
Balances, December 31, 2010	94,822,593	948	149,417	(192,585)	(42,220)
Issuance of common stock from private placement, net of issuance costs	36,978,440	370	20,029	—	20,399
Issuance of common stock from exercise of stock options	150,000	2	56	—	58
Initial value of warrant liability	—	—	(6,356)	—	(6,356)
Stock-based compensation	—	—	522	—	522
Net loss	—	—	—	(6,942)	(6,942)
Balances, December 31, 2011	131,951,033	1,320	163,668	(199,527)	(34,539)
Stock-based compensation	—	—	947	—	947
Net loss	—	—	—	(8,277)	(8,277)
Balances, December 31, 2012	131,951,033	$1,320	$164,615	$(207,804)	$(41,869)

See accompanying notes consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2012	2011	2010
OPERATING ACTIVITIES:			
Net loss	$ (8,277)	$ (6,942)	$ (9,593)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	95	86	212
Amortization of debt issuance costs	419	419	418
Stock-based compensation	947	522	385
Change in fair value of warrant liability	(1,898)	(2,201)	—
Changes in operating assets and liabilities:			
Accounts receivable, net	(2,686)	788	(215)
Prepaid expenses and other current assets	(132)	3	142
Accounts payable	(26)	371	46
Accrued liabilities	1,124	(100)	151
Accrued compensation and related expense	156	358	(348)
Accrued royalties	140	72	245
Accrued interest	(133)	(2,205)	438
Deferred revenues	—	(75)	—
Net cash used in operating activities	(10,271)	(8,904)	(8,119)
INVESTING ACTIVITIES:			
Purchase of property and equipment	(127)	(184)	(150)
Decrease (increase) in short-term investments	16,496	(19,496)	12,500
Net cash provided by (used in) investing activities	16,369	(19,680)	12,350
FINANCING ACTIVITIES:			
Issuance of common stock from private placement, net of issuance costs	—	20,399	—
Issuance of common stock from exercise of options and employee purchase plan, net of issuance costs	—	58	21
Payment of secured notes payable	(6,675)	(1,442)	—
Payment of capital lease obligation	—	—	(5)
Net cash provided by (used in) financing activities	(6,675)	19,015	16
Net increase (decrease) in cash and cash equivalents	(577)	(9,569)	4,247
Cash and cash equivalents at beginning of year	1,900	11,469	7,222
Cash and cash equivalents at end of year	$ 1,323	$ 1,900	$11,469
Supplemental disclosure of cash flow information:			
Interest received	$ 17	$ 28	$ 21
Interest paid	$ 9,224	$ 11,981	$ 9,411
Income taxes	$ 1	$ 1	$ 1

See accompanying notes to consolidated financial statements.

InSite Vision Incorporated

Notes to Consolidated Financial Statements
For the years ended December 31, 2012, 2011 and 2010

1. Business and Summary of Significant Accounting Policies

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

The Company's DuraSite sustained drug delivery technology is a proven synthetic polymer-based formulation designed to extend the residence time of a drug relative to conventional topical therapies. It enables topical delivery of a drug as a solution, gel or suspension and can be customized for delivering a wide variety of drug candidates. The Company has focused its research and development and commercial support efforts on topical products formulated with the DuraSite drug delivery technology.

The Company has incurred significant losses since inception, including net losses of approximately $8.3 million, $6.9 million and $9.6 million for the years ended December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012, the Company's accumulated deficit was $207.8 million.

The Company believes it has available funds to enable us to meet our obligations for approximately the next 12 months. Our ability to fund our operations is dependent primarily upon our ability to execute on our business plan, including generating sufficient cash inflows from operating activities and obtaining additional funding.

The Company will need to raise additional funding to support our operating activities. Adequate funding may not be available on acceptable terms, or at all. The failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition. The accompanying financial statements do not include any adjustments that might result from the outcome of these uncertainties.

Principles of Consolidation. The consolidated financial statements include the accounts of InSite Vision Incorporated as well as its wholly-owned subsidiaries. All intercompany transactions have been eliminated in consolidation.

Industry Segment and Geographic Information. The Company operates in one segment and is focused on developing drugs and drug delivery systems principally for ophthalmic indications. The Company had limited foreign-based operations for the years ended December 31, 2012, 2011 and 2010. All long-lived assets are located in the United States.

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 materially from those estimates.

Reclassifications. Certain amounts in prior years' financial statements have been reclassified to conform to the current presentation. These reclassifications had no impact on previously reported results of operations or stockholders' deficit.

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.

Short-term investments. The Company considers all investments with original maturities of 12 months or less from the date of purchase to be short-term investments. They are classified as trading securities principally bought and held for the purpose of selling them in the near term, with unrealized gains and losses included in earnings.

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, 2012, 2011 and 2010 was $95,000, $86,000 and $212,000, respectively. The costs of repairs and maintenance are expensed as incurred.

Impairment of Long-Lived Assets. The Company periodically assesses the recoverability of its long-lived assets for which an indicator of impairment exists by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If the Company concludes that the carrying value will not be recovered, the Company measures the amount of such impairment by comparing the fair value to the carrying value. For the years ended December 31, 2012, 2011 and 2010, no impairment of property and equipment was recorded.

Patents. As a result of the Company's research and development efforts, the Company has obtained, or is applying for, a number of patents to protect proprietary technology and inventions. All costs associated with patents for product candidates under development are expensed as incurred. As of December 31, 2012, the Company had no capitalized patent costs.

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 years ended December 31, 2012, 2011 and 2010 were $419,000, $419,000 and $418,000, respectively, and are included in interest expense and other, net in the Consolidated Statements of Operations. See Note 7, "Non-Recourse Secured Notes Payable" for further discussion of the underlying debt.

Warrant Liability. The Company issued warrants to purchase shares of the Company's common stock in connection with a private placement financing transaction in July 2011. The Company accounted for these warrants as a liability measured at fair value due to a provision included in the warrant agreements that provides the warrant holders with an option to require the Company (or its successor) to purchase their warrants for cash in the event of a "Fundamental Transaction" (as defined in the warrant agreements). The actual amount of cash required if the option is exercised would be determined using the Black-Scholes Option Pricing Model (the "Black-Scholes Model") as determined in accordance with the terms of the warrant agreements. The fair value of the warrant liability is estimated using the Black-Scholes Model, which requires inputs such as the remaining term of the warrants, share price volatility and risk-free interest rate. These assumptions are reviewed on a monthly basis and changes in the estimated fair value of the outstanding warrants are recognized each reporting period in the Consolidated Statements of Operations under "Change in fair value of warrant liability."

Fair Value Measurements. Fair value is the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Fair value is estimated by applying the following hierarchy, which prioritizes the inputs used to measure fair value into three levels and bases the categorization within the hierarchy upon the lowest level of input that is available and significant to the fair value measurement:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than quoted prices in active markets for identical assets and liabilities, quoted prices for identical or similar assets or liabilities in inactive markets, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Inputs that are generally unobservable and typically reflect management's estimate of assumptions that market participants would use in pricing the asset or liability.

As of December 31, 2012 and 2011, $9.2 million and $26.3 million, respectively, of the Company's cash, cash equivalents and short-term investments consisted of Level 1 Treasury-backed money market funds that are measured at fair value on a recurring basis.

The Company's financial instruments consist mainly of cash and cash equivalents, short-term investments, accounts receivable, accounts payable, accrued liabilities and debt obligations. 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 those of 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.

The Company has debt in the form of non-recourse, secured notes payable with a fixed interest rate, which constitute $51.9 million of Level 2 borrowings outstanding at December 31, 2012, measured at fair value on a nonrecurring basis, with an interest rate of 16%. At December 31, 2012, the Company's debt was reflected in the accompanying consolidated financial statements at face value. Due to a decline in and uncertainty regarding AzaSite earned royalty revenues, it is reasonably possible that the fair value of the debt has declined. The decline in value of debt is not reasonably determinable at this time.

As discussed above, the fair value of the warrant liability, determined using Level 3 criteria, was initially recorded on the grant date and remeasured at December 31, 2012 and 2011 using the Black-Scholes Model, which requires inputs such as the remaining term of the warrants, share price volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop.

The fair value of the warrant liability was estimated using the following assumptions, as determined in accordance with the terms of the warrant agreements, at December 31, 2012 and 2011:

	December 31, 2012	December 31, 2011
Risk-free interest rate	0.4%	0.8%
Remaining term (years)	3.5	4.5
Expected dividends	0.0%	0.0%
Volatility	100.0%	100.0%

The expected dividend yield is set at zero because the Company has never paid cash dividends and has no present intention to pay cash dividends. Per the terms of the warrant agreements, expected volatility is based on the historical volatility of the Company's common stock and is equal to the greater of 100% or the 30-day volatility rate. The risk-free interest rates are taken from the Daily Federal Yield Curve Rates as published by the Federal Reserve and represent the yields on actively-traded U.S. Treasury securities for a term equal to the remaining term of the warrants.

The following table provides a summary of changes in the fair value of the Company's Level 3 financial liabilities for the year ended December 31, 2012 (in thousands):

Balance at December 31, 2011	$ 4,155
Net decrease in fair value of warrant liability on remeasurment	(1,898)
Balance at December 31, 2012	$ 2,257

The net decrease in the estimated fair value of the warrant liability was recognized as income under "Change in fair value of warrant liability" in the Consolidated Statements of Operations.

Revenue Recognition. The Company recognizes revenue when four basic criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured. The Company has arrangements with multiple revenue-generating elements. The Company analyzes its multiple element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting. An item can generally be considered a separate unit of accounting if both of the following criteria are met: the delivered item(s) has value to the customer on a stand-alone basis and if the arrangement includes a general right of return and delivery or performance of the undelivered item(s) is considered probable and substantially in the control of the Company. Items that cannot be divided into separate units are combined with other units of accounting, as appropriate. Consideration received is allocated among the separate units based on the unit's selling price and is recognized in full when the criteria are met. The Company deems service to be rendered if no continuing obligation exists on the part of the Company.

The Company's revenues are primarily derived from royalties on product sales and licensing agreements, and such agreements may provide for various types of payments, including upfront payments, research funding and related fees during the terms of the agreements, milestone payments based on the achievement of established development objectives and licensing fees.

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 collectability is reasonably assured.

Revenues associated with non-refundable up-front license fees under arrangements where the license fees cannot be accounted for as separate units of accounting are deferred and recognized as revenues on a straight-line basis over the expected term of the Company's continued involvement. Revenues from the achievement of milestones are recognized as revenues when the milestones are achieved and the milestone payments are due and collectible.

For the year ended December 31, 2011, the Company adopted amendments to the accounting standard related to multiple-deliverable revenue arrangements. The amendment requires entities to allocate revenue in multiple-deliverable revenue arrangements using estimated selling prices of the delivered goods and services based on a selling price hierarchy. The amendment eliminated the residual method of revenue allocation and requires revenue to be allocated using the relative selling price method. The adoption of this amendment did not impact the Company's consolidated financial position or results of operations since the Company did not enter into or materially modify revenue arrangements for the years ended December 31, 2012 and 2011. In addition, there have been no significant changes to the units of accounting, the allocation of consideration received to the various units of accounting, and the timing of revenue recognition based on this amendment. The Company does not expect the adoption of this amendment to have a material impact on future periods.

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's research and development activities. The Company expenses these research and development activities 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 Expenses. General and administrative expenses include salaries, benefits, facility costs, services provided by outside consultants and contractors, legal services, 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.

Cost of Revenues. The Company recognizes royalties to third parties and the cost of inventory shipped related to the sale of the Company's products when they are incurred.

Stock-Based Compensation. The Company's stock-based compensation programs consist of stock options granted to employees as well as our employee stock purchase plan, based on the grant date fair value of those awards.

The grant date fair value of the award is recognized as expense over the requisite service period. The Company uses the Black-Sholes option pricing model to compute the estimated fair value of stock option awards. Using this model, fair value is calculated based on assumptions with respect to: expected volatility of our common stock price: the periods of time over which employees and members of our board are expected to hold their options prior to exercise; expected dividend yield on our common stock; and risk-free interest rates. Stock-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. The estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

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

The Company occasionally 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, 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 $56,000 and $20,000 during the years ended December 31, 2012 and 2011, respectively. No such charges were incurred in 2010.

Net Loss 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 2012, 2011 and 2010 as their inclusion would be anti-dilutive.

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)	2012	2011	2010
Numerator:			
Net loss	$ (8,277)	$ (6,942)	$ (9,593)
Denominator:			
Weighted-average shares outstanding	131,951	111,769	94,774
Effect of dilutive securities:			
Stock options and warrants	—	—	—
Weighted-average shares outstanding for diluted loss	131,951	111,769	94,774
Net loss per share:			
Basic	$ (0.06)	$ (0.06)	$ (0.10)
Diluted	$ (0.06)	$ (0.06)	$ (0.10)

For the years ended December 31, 2012, 2011 and 2010, 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, 2012, 2011 and 2010, 28,156,898, 25,795,339 and 10,293,478 options and warrants, respectively, were excluded from the calculation of diluted earnings per share because the effect was anti-dilutive.

Comprehensive Income (Loss). Comprehensive income (loss) is the change in equity from transactions and other events and circumstances other than those resulting from investments by owners and distributions to owners. The consolidated comprehensive loss for the Company was equal to the net loss attributable to the Company for the years ended December 31, 2012, 2011 and 2010.

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. The Company accounts for income taxes under the liability method; under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax reporting bases of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Realization of deferred tax assets is dependent upon future earnings, the timing and amount of which are uncertain.

The Company utilizes a two-step approach to recognize and measure uncertain tax positions, if any. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained upon tax authority examination, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement.

Significant Customers and Risk. All revenues recognized and/or deferred were primarily from AzaSite licensees. The Company is entitled to receive royalty revenues from net sales of AzaSite under the terms of its agreements with Merck and other licenses 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. Revenues from Merck represented approximately 90%, 90% and 92% of total revenues for the years ended December 31, 2012, 2011 and 2010, respectively.

Credit Risk. Financial instruments that potentially subject the Company to significant concentrations of credit risk consist principally of cash, cash equivalents and short-term investments. The Company's cash, cash equivalents and short-term investments are primarily deposited in demand accounts with two financial institutions.

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. Accordingly, delays in the manufacture of the Company's product candidates or the active pharmaceutical ingredients could adversely impact the development of the Company's product candidates. Furthermore, the Company has no control over the manufacture and the overall product supply chain of products for which it is entitled to receive revenue.

2. License Agreements

In December 2003, the Company completed the sale of its drug candidate for the treatment of ocular infections to Bausch & Lomb Incorporated ("Bausch & Lomb"), pursuant to a Purchase Agreement and a License Agreement. The drug candidate, Besivance, was developed by Bausch & Lomb. In May 2009, the FDA

approved Besivance to treat bacterial conjunctivitis (pink eye). Besivance was launched in the United States by Bausch & Lomb in the last half of 2009. In 2011, Besivance was launched internationally in select countries. During the years ended December 31, 2012, 2011 and 2010, the Company recognized $2,126,000, $1,208,000 and $467,000, respectively, of royalties related to net sales of Besivance by Bausch & Lomb.

On February 15, 2007, the Company entered into a license agreement for AzaSite™ (the "Merck License") with Inspire Pharmaceuticals, Inc ("Inspire"). In May 2011, Merck & Co. ("Merck") acquired Inspire and Inspire became a wholly-owned subsidiary of Merck. Under the Merck License, the Company licensed to Merck, 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 Merck an exclusive sublicense under the Pfizer patent rights the Company has licensed under the Pfizer License discussed below. Merck has the right to grant sublicenses under the terms of the Merck License.

Merck 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. Food and Drug Administration ("FDA"). Merck also pays the Company a royalty on net sales of AzaSite in the United States and Canada. The royalty rate is currently 25% of net sales. Merck is obligated to pay the Company royalties under the Merck License for the longer of (i) eleven years from the launch of the first product or (ii) the period during which a valid claim under a patent exists. Until September 30, 2013, Merck 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 under the Merck License or in the event that Merck is required to pay license fees to third parties for the continued use of AzaSite. Merck may also terminate the Merck License at any time upon 6 months notice.

The Company also entered into a supply agreement (the "Supply Agreement") with Merck 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 this active ingredient. The Supply Agreement was terminated in July 2012.

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 Merck License, 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.

On August 9, 2012, the Company amended the payment terms of the existing Merck License. Under the amended terms, on a quarterly basis, Merck will pay the Company the higher of the pro-rata annual minimum royalty or the earned royalty for 2012 and 2013. In addition, in August 2012, Merck paid the Company a $7.3 million catch-up payment for the difference between the earned royalties already paid for the fourth quarter of 2011 and the first and second quarters of 2012, and the pro-rata annual minimum royalties for those quarters. For the fiscal year ended September 30, 2011, the measurement period pursuant to the terms of the Merck License, the Company received $15 million in minimum royalties from Merck. For the fiscal year ended September 30, 2012, the Company received $17 million in minimum royalties from Merck. For the fiscal year ending September 30, 2013, the Company expects to receive $19 million in minimum royalties, unless Merck cancels the agreement upon six months notice.

In August 2007, Merck commercially launched AzaSite in the United States. Accordingly, during the years ended December 31, 2012, 2011 and 2010, the Company recognized $19,515,000, $13,930,000 and $10,652,000, respectively, of royalties related to the Merck License. Additionally, during the years ended December 31, 2011 and 2010, the Company recognized $449,000 and $258,000, respectively, of revenue from Merck for the sales of the active ingredient, azithromycin, under the Supply Agreement, sales of AzaSite inventory and for contract services provided by the Company.

On February 15, 2007, the Company entered into a worldwide, exclusive, royalty-bearing license agreement with Pfizer Inc. ("Pfizer") under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus (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 Merck. Based on the royalty report provided by Merck, for the years ended December 31, 2012, 2011 and 2010, the Company recorded third-party royalties of $1,062,000, $1,407,000 and $1,491,000, respectively, due primarily under the Pfizer License.

The Company has entered into, and will continue to pursue additional licensing agreements, corporate collaborations and service contracts. There can be no assurance that the Company will be able to negotiate acceptable collaborative, licensing or service agreements, or that the existing arrangements will be successful or renewed or will not be terminated.

3. Short-term Investments

As of December 31, 2012 and 2011, the Company had $8.0 million and $24.5 million in short-term investments, respectively. The Company's investment policy is to limit the risk of principal loss and to ensure safety of invested funds by generally attempting to limit market risk. Accordingly, the Company's short-term investments were invested in U.S. Treasury securities with original maturities of 12 months or less. They are classified as trading securities principally bought and held for the purpose of selling them in the near term, with unrealized gains and losses included in earnings. At December 31, 2012 and 2011, the unrealized gains on these short-term investments were insignificant.

4. Accounts Receivable, net

Accounts receivable, net represent amounts due to the Company from its licensees, including Merck and other third parties. Accounts receivable, net increased by $2.7 million for the year ended December 31, 2012 from December 31, 2011. Increase primarily resulted from an additional $2.6 million minimum royalty true-up by Merck. At December 31, 2012 and 2011, the Company did not record a bad debt allowance related to any accounts receivable as all amounts were reasonably expected to be collected. The need for a bad debt allowance is evaluated each reporting period based on the Company's assessment of the collectability of the amounts.

5. Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2012	**2011**
Laboratory and other equipment	$ 1,399	$1,272
Leasehold improvements	45	45
Furniture and fixtures	14	14
	1,458	1,331
Accumulated depreciation and amortization	(1,081)	(986)
Property and equipment, net	$ 377	$ 345

6. Warrant Liability

On July 18, 2011, the Company completed a private placement financing transaction in which it sold shares of its common stock and warrants to purchase shares of its common stock. The Company sold a total of

36,978,440 shares of common stock, at a price of $0.60 per share, and issued warrants to purchase up to 14,791,376 shares of common stock. The warrants are exercisable at $0.75 per share and expire five years from the date of issuance. The private placement resulted in $22.2 million in gross proceeds and approximately $20.4 million in net proceeds to the Company after deducting placement agent fees, legal, accounting and other costs associated with the transaction. The Company has used the net proceeds of the transaction to fund clinical trials and for general corporate purposes, including working capital.

As discussed in Note 1, the warrants issued in July 2011 include a provision that provides the warrant holders with an option to require the Company (or its successor) to purchase the warrants for cash in an amount equal to the Black-Scholes value in the event of a "Fundamental Transaction" (as defined in the warrant agreements). Accordingly, the fair value of the warrants at the issuance date was estimated using the Black-Scholes Model, as determined in accordance with the terms of the warrant agreements, and the Company recorded a warrant liability of $6.4 million. The Company remeasured the warrant liability at December 31, 2012 and 2011, and recorded a decrease to the warrant liability of approximately $1.9 million and $2.2 million, respectively, which was recognized as income in the Company's Consolidated Statement of Operations for the year ended December 31, 2012 and 2011. Additional disclosures regarding assumptions used in calculating the fair value of the warrant liability are included in Note 1.

7. Non-Recourse 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 Merck from minimum required royalties and royalties from net 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. As of December 31, 2012, no balance remained in the interest reserve. Further shortfalls, if any, may be paid by the Company to avoid default under the agreement but the Company currently has no plans to do so. The notes may be redeemed at the Company's option at the current principal amount. As of December 31, 2012, $41.5 million of secured notes payable was classified as long-term and $10.4 million was classified as current.

At December 31, 2012, the estimated future principal payments on the notes, based on minimum royalty income covered by the agreement and future projected sales, were as follows (in thousands):

Year Ending December 31,	
2013	$10,395
2014	—
2015	—
2016	—
2017	—
Thereafter	41,488
Total secured notes payable	$51,883

At the current level of AzaSite royalties received by the Company from Merck, the Company will default on the notes during 2014 after the receipt of the final minimum royalty payment in the fourth quarter of 2013. Based on current royalty levels, the royalties thereafter will not cover the required interest payments. After default and assuming foreclosure by the noteholders, the Company will lose its right to receive AzaSite royalties in North America and the principal balance of the notes will be recorded as income and the note liability will be eliminated from the Consolidated Balance Sheet.

8. Commitments and Contingencies

The Company has entered into certain license agreements that require it to make royalty payments for the life of the licensed patents. The estimated royalty payments related to the net sales of AzaSite in North America are approximately $4.8 million for the period 2013 through 2019. These contractual obligations are reflected in the Company's financial statements once the related obligation becomes due. Much of these obligations would be eliminated if the Company defaults on the notes, as the noteholders will be responsible for paying these royalties.

The Company conducts its operations from leased facilities in Alameda, California under non-cancelable operating lease agreements that expire in December 2013. Lease payments include rent and the Company's pro-rata share of operation expenses. The Company subleases a portion of the facility under a lease agreement that expires in 2013. Lease income includes rent and a pro-rata share of operation expenses. For accounting purposes, the Company is amortizing all rent payments and receipts ratably over the life of the lease. Rent expense for the years ended December 31, 2012, 2011 and 2010, was $697,000, $697,000, and $757,000, respectively. Future minimum lease payments under the operating lease and future cash receipts from the sublease, are as follows (in thousands):

Year Ending December 31,	Operating Lease Cash Payments	Operating Sublease Cash Receipts	Operating Lease Cash Payments, net
2013	$848	$106	$742

9. Income Taxes

Provision for Income Taxes

There was no provision for income taxes for the years ended December 31, 2012, 2011 and 2010 due to the Company's net operating losses.

Income tax provision related to continuing operations differ from the amounts computed by applying the statutory income tax rate of 34% to pretax loss as follows (in thousands):

	2012	2011	2010
Tax provision at federal statutory rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	0.0%	0.0%	0.0%
Warrant liability	7.8%	10.8%	0.0%
Other permanent differences	0.0%	-0.1%	-1.4%
Credits	0.0%	2.7%	0.9%
Expiring net operating losses	-15.0%	-11.4%	-46.0%
True up of deferred tax assets	0.0%	-4.3%	0.0%
Valuation allowance	-26.8%	-31.7%	12.5%
Effective tax rate	0.0%	0.0%	0.0%

Deferred Tax Assets and Liabilities

Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets for federal and state income taxes as of December 31, 2012 and 2011 were as follows (in thousands):

	2012	2011
Deferred tax assets:		
Net operating loss carryforwards	$ 44,077	$ 40,138
Tax credit carryforwards	7,870	7,523
Capitalized research and development	9,926	14,163
Depreciation	182	263
Other	581	291
Total deferred tax assets	62,636	62,378
Valuation allowance	(62,636)	(62,378)
Net deferred tax assets	$ —	$ —

Realization of our deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Because of our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance. During the years ended December 31, 2012 and 2011, the valuation allowance increased by $0.3 million and $1.9 million, respectively.

At December 31, 2012, the Company had net operating loss carryforwards for federal income tax purposes of approximately $113.4 million, which expire in the years 2013 through 2032 and federal tax credits of approximately $3.3 million, which expire in the years 2018 through 2032. At December 31, 2012, the Company also had net operating loss carryforwards for state income tax purposes of approximately $91.9 million, which expire in the years 2013 through 2032, and state research and development tax credits of approximately $4.6 million, which carryforward indefinitely.

The future utilization of the Company's net operating loss 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 the Company has any additional ownership changes in the future.

The valuation allowance includes amounts of benefit at both December 31, 2012 and 2011 related to stock-based compensation and exercises, prior to the implementation of Accounting Standards Codification 515 and 718 that will be credited to additional paid-in capital when realized.

The American Taxpayer Relief Act of 2012 was signed into law on January 2, 2013. The act retroactively reinstated various expired tax extenders for the 2012 year. None of the extenders included in the Act are material to our financial statements and the impact of the tax law change will be accounted for in 2013 under ASC 740-10-45-15 as this is the period of enactment.

A change in California law occurred in November 2012 with the enactment of RTC Sec. 25128.7 related to apportionment of income. The new law is effective beginning in 2013. All California deferred tax assets have been adjusted using the rates that will be in effect when the deferred tax assets are expected to be utilized.

Unrecognized Tax Benefits

The Company has incurred net operating losses since inception and does not have any unrecognized tax benefits. The Company's policy is to include interest and penalties related to unrecognized tax benefits, if any, within the provision for taxes in the consolidated statements of operations. If the Company is eventually able to recognize its uncertain positions, its effective tax rate would be reduced. The Company currently has a full valuation allowance against its net deferred tax assets which would impact the timing of the effective tax rate benefit should any uncertain tax positions be favorably settled in the future. Any adjustments to the Company's uncertain tax positions would result in an adjustment of its net operating loss or tax credit carry forwards.

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 2009 for federal returns and 2008 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.

Although it is reasonably possible that certain unrecognized tax benefits may increase or decrease within the next twelve months due to tax examination changes, settlement activities, expirations of statute of limitations, or the impact on recognition and measurement considerations related to the results of published tax cases or other similar activities, the Company does not anticipated any significant changes to unrecognized tax benefits over the next 12 months. During the years ended December 31, 2012 and 2011, no interest or penalties were required to be recognized relating to unrecognized tax benefits.

10. Common Stock Warrants

The following table shows outstanding warrants as of December 31, 2012, all of which were issued in the July 2011 private placement financing transaction. All of the outstanding warrants have cashless exercise provisions in the event the registration statement registering the resale of the shares of common stock issuable upon exercise of the warrants is not effective or the prospectus forming a part of the registration statement is not current. All warrants are exercisable for common stock.

Date Issued	Warrant Shares	Exercise Price	Expiration Date	Cash if Exercised
July 18, 2011	14,791,376	$0.75	July 18, 2016	$11,093,532

11. Stock-based Compensation

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 grant 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.

Employee Stock Purchase Plans

The Company maintained an employee stock purchase plan, adopted in 1994 and amended thereafter (the "Purchase Plan"), until August 2009. In August 2009, the Purchase Plan was suspended. No new offering period will commence and no additional shares will be added to the Purchase Plan under its evergreen provision unless and until approved by the Company's Board of Directors. The Purchase Plan operated in 24-month "offering periods" that are each divided into four six-month "purchase periods." The Purchase Plan allowed 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 were limited to 10% of each employee's eligible compensation, subject to certain Internal Revenue Service restrictions. All of the Company's employees were eligible to participate in the Purchase Plan after certain service periods were met. The number of shares available for issuance under the Purchase Plan was 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. No shares have been issued under the Purchase Plan since 2009. As of December 31, 2012, there was no remaining unrecorded deferred stock-based compensation expense related to the Purchase Plan. As of December 31, 2012, 515,183 shares were reserved for issuance under the Purchase Plan.

Stock-based Compensation

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 years ended December 31, 2012, 2011 and 2010 was as follows (in thousands):

	Year Ended December 31,		
	2012	2011	2010
Stock-based compensation expense by type of award:			
Employee stock options	$891	$502	$385
Scientific Advisory Board stock options	56	20	—
Total stock-based compensation	$947	$522	$385

Stock-based compensation included in expense line items in the Consolidated Statements of Operations for the year ended December 31, 2012, 2011 and 2010 was as follows (in thousands):

	Year Ended December 31,		
	2012	2011	2010
Research and development	$271	$141	$ 74
General and administrative	676	381	311
	$947	$522	$385

During the years ended December 31, 2012 and 2011, respectively, the Company granted options to purchase 4,047,500 and 2,955,000 shares of common stock with an estimated total grant date fair value of $1.2 million and $0.9 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 years ended December 31, 2012 and 2011, the Company estimated that the stock-based compensation for the awards not expected to vest was $0.2 million and $0.3 million, respectively.

As of December 31, 2012 and 2011, the unrecorded deferred stock-based compensation balances related to stock options were $1.3 million and $1.4 million, respectively, and will be recognized over an estimated weighted-average amortization period of 2.2 years and 2.5 years, respectively.

Fair Value Assumptions

The fair value of each option grant is estimated using the Black-Scholes valuation model on the date of grant and the graded-vesting method with the following weighted-average assumptions:

	Year ended December 31,		
Stock Options	**2012**	**2011**	**2010**
Risk-free interest rate	0.7%	0.9%	2.0%
Expected term (years)	5	5	5
Expected dividends	0.0%	0.0%	0.0%
Volatility	90.9%	89.7%	87.8%

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.

The following is a summary of activity under the Company's stock option 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, 2009	7,406,285	$0.74	4.93	$296
Granted	5,424,374	0.37		
Exercised	(84,193)	0.24		
Forfeited	(325,804)	0.34		
Expired	(3,485,199)	1.08		
Outstanding at December 31, 2010	8,935,463	0.40	8.79	211
Granted	2,955,000	0.44		
Exercised	(150,000)	0.38		
Forfeited	(455,000)	0.33		
Expired	(281,500)	0.70		
Outstanding at December 31, 2011	11,003,963	0.41	8.11	861
Granted	4,047,500	0.42		
Exercised	—	0.00		
Forfeited	(784,223)	0.37		
Expired	(901,718)	0.38		
Outstanding at December 31, 2012	13,365,522	$0.42	7.69	$156
Options vested and expected to vest at December 31, 2012	12,923,912	$0.42	7.64	$156
Options exercisable at December 31, 2012	7,752,944	$0.42	7.02	$150

At December 31, 2012, the Company had 5,614,796 shares of common stock available for grant under its 2007 Plan. The weighted average grant date fair value of options granted during the years ended December 31, 2012, 2011 and 2010 were $0.29, $0.31 and $0.25, respectively. The total intrinsic value of options exercised during the year ended December 31, 2011 and 2010 were $24,000 and $13,000, respectively. No options were exercised during the year ended December 31, 2012.

At December 31, 2011 and 2010 options to purchase 4,718,014 and 2,889,719 shares of common stock were exercisable at weighted-average exercise prices of $0.43 and $0.52, per share, respectively.

12. Legal Proceedings

The Company is subject to various claims and legal actions during the ordinary course of its business. On November 30, 2009, a patent interference was declared before the Board of Patent Appeals and Interferences on certain U.S. patents covering AzaSite. Regents of the University of California, or University, assert that the inventions contained in these patents were made by a former employee of the University alone, and without collaboration with us. They are asserting that they own those inventions, and that they are entitled to an award of priority of invention and a judgment that the inventions are not patentable to us. On November 25, 2011, the U.S. Patent and Trademark Office, or USPTO, entered judgment against the University. On December 23, 2011, the University filed a Notice of Appeal to the Court of Appeals for the Federal Circuit in Washington, D.C., and on January 4, 2012, we filed a Notice of Cross-Appeal. Oral arguments took place in November 2012 and no decision has yet been rendered. We continue to believe the University's assertions are without merit and we will continue to vigorously defend our position.

The Company received a Notice Letter that Sandoz, Inc. or Sandoz, has filed an Abbreviated New Drug Application, or ANDA, with the FDA seeking marketing approval for a 1% azithromycin ophthalmic solution, or the Sandoz Product, prior to the expiration of the five U.S. patents listed in the Orange Books for AzaSite, which include four of our patents and one patent licensed to us by Pfizer. In the paragraph IV Certification accompanying the Sandoz ANDA filing, Sandoz alleges that the claims of the Orange Book listed patents are invalid, unenforceable and/or will not be infringed upon by the Sandoz Product. On May 26, 2011, we, Merck and Pfizer filed a patent infringement lawsuit against Sandoz and related entities. The plaintiff companies have agreed that Merck will take the lead in prosecuting this lawsuit. The filing of this lawsuit triggered an automatic stay, or bar, of the FDA's approval of the ANDA for up to 30 months or until a final district court decision of the infringement lawsuit, whichever comes first. We and the other plaintiffs intend to vigorously enforce our patent rights relating to AzaSite and vigorously contest any Sandoz assertions that these patents are invalid or unenforceable.

On January 3, 2013, Janel Joseph and Mitchell Joseph III filed a complaint in circuit court in Fayette County, Kentucky against Bausch & Lomb and the Company alleging that Janel Joseph was injured when her physician treated her with the Bausch & Lomb product Besivance following a photorefractive keratectomy. The plaintiffs allege that the use was off-label but nonetheless marketed by the defendants. Ms. Joseph alleges loss of vision and Mr. Joseph, her husband, alleges loss of consortium. On February 1, 2013, Bausch & Lomb removed the case to the United States District Court for the Eastern District of Kentucky. On February 8. 2013, the defendants filed answers denying the allegations. There have been no further proceedings. The plaintiffs to date have not made a specific claim for damages.

There are currently no other claims or legal actions that would have a material adverse impact on our financial position, operations or potential performance.

13. Quarterly Results (Unaudited)

The following table is a summary of the quarterly results of operations for the years ended December 31, 2012 and 2011. 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 Company's operating results for any quarter are not necessarily indicative of results for any future period.

	2012			
(In thousands, except per share amounts)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	$ 2,273	$ 1,816	$12,139	$ 5,413
Cost of revenues	265	186	313	298
Gross profit	2,008	1,630	11,826	5,115
Income (loss) from operations	(3,412)	(4,513)	7,603	(359)
Net income (loss)	(4,847)	(6,754)	5,142	(1,818)
—basic	$ (0.04)	$ (0.05)	$ 0.04	$ (0.01)
—diluted	$ (0.04)	$ (0.05)	$ 0.04	$ (0.01)

	2011			
(In thousands, except per share amounts)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	$ 3,110	$ 3,069	$6,613	$ 3,131
Cost of revenues	577	368	343	629
Gross profit	2,533	2,701	6,270	2,502
Income (loss) from operations	124	(212)	2,695	(1,583)
Net income (loss)	(2,440)	(2,773)	1,511	(3,240)
—basic	$ (0.03)	$ (0.03)	$ 0.01	$ (0.02)
—diluted	$ (0.03)	$ (0.03)	$ 0.01	$ (0.02)

14. Subsequent Events

The Company evaluated subsequent events through the date on which the financial statements were issued, and has determined that there are no subsequent events that require adjustments or disclosure to the financial statements for the year ended December 31, 2012.

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 Exchange Act, as of the end of the period covered by this report (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, 2012. 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, 2012, 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, 2012 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On July 26, 2012, in connection with Merck entering into a supply agreement with a third-party supplier of azithromycin, Merck and the Company terminated the Supply Agreement.

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 2012," "Compensation, Discussion and Analysis," "Compensation of Named Executive Officers," "Summary Compensation Table for 2010," "Grants of Plan Based Awards in 2012," "Outstanding Equity Awards at Fiscal 2012 Year End," " Option Exercises and Stock Vested in 2012," "Non-Qualified Deferred Compensation for 2012," "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

Independent Auditor 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 Item 8 of Part II 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" 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 26, 2013

INSITE VISION INCORPORATED

By: /s/ LOUIS DRAPEAU

Louis Drapeau
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PEOPLE BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Louis C. Drapeau, his attorney in fact and agent, with the power of substitution and resubstition, for him and in his 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 might or could do in person, hereby ratifying and confirming all that said attorney in fact, or his 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/ TIMOTHY RUANE **Timothy Ruane**	Chief Executive Officer and Director (Principal Executive Officer)	March 26, 2013
/s/ LOUIS DRAPEAU **Louis Drapeau**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 26, 2013
/s/ BRIAN LEVY **Brian Levy, O.D. M.Sc.**	Director	March 26, 2013
/s/ TIMOTHY MCINERNEY **Timothy McInerney**	Chairman of Board, Director	March 26, 2013
/s/ ROBERT O'HOLLA **Robert O'Holla**	Director	March 26, 2013
/s/ CRAIG A. TOOMAN **Craig A. Tooman**	Director	March 26, 2013
/s/ ANTHONY J. YOST **Anthony J. Yost**	Director	March 26, 2013

EXHIBIT INDEX

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 December 14, 2011.
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[8HH]	Form of Nonqualified Stock Option Agreement (2007).
10.5[8HH]	Form of Incentive Stock Option Agreement (2007).
10.6[10HH]	Form of Indemnification Agreement between the Company and its directors and officers.
10.7[11HH]	Form of Employee's Proprietary Information and Inventions Agreement.
10.8[12]	Facilities Lease, dated September 1, 1996, between the Registrant and Alameda Real Estate Investments.
10.9[13]	Amendment No. 1 to Marina Village Office Tech Lease, dated July 20, 2001 and effective January 1, 2002.
10.10[5]	Amendment No. 3 to Marina Village Office Tech Lease, dated November 28, 2006.
10.11[14H]	Exclusive License Agreement, dated as of February 15, 2007, by and between the Company and Pfizer, Inc. and Pfizer Products, Inc.
10.12[14H]	License Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.13[14H]	Trademark License Agreement, dated as of February 15, 2007, by and between the Company and Inspire Pharmaceuticals, Inc.
10.14[15H]	First Amendment to License Agreement, dated as of August 9, 2012, by and between the Company and Inspire Pharmaceuticals, Inc.

Number	Exhibit Table
10.15[16]	Purchase and Sale Agreement, dated as of February 21, 2008, by and between Azithromycin Royalty Sub LLC and the Company.
10.16[16]	Note Purchase Agreement, dated as of February 21, 2008, by and among Azithromycin Royalty Sub LLC, the Company and the purchasers named therein.
10.17[16]	Indenture, dated as of February 21, 2008, by and between Azithromycin Royalty Sub LLC and U.S. Bank National Association.
10.18[16]	Pledge and Security Agreement made by the Company to U.S. Bank National Association, as Trustee, dated February 21, 2008.
10.19[16]	Residual License Agreement by and between Azithromycin Royalty Sub LLC and the Company dated February 21, 2008.
10.20[17HH]	InSite Vision Incorporated Annual Bonus Plan.
10.21[18HH]	InSite Vision Incorporated Severance Plan.
10.22[19HH]	Offer letter, by and between the Company and Louis Drapeau, dated October 31, 2008.
10.23[20HH]	Offer letter, by and between the Company and Timothy Ruane, dated December 1, 2010.
10.24[21]	Form of Securities Purchase Agreement, dated July 12, 2011.
10.25[21]	Form of Common Stock Warrant issued pursuant to Securities Purchase Agreement, dated July 12, 2011.
10.25[22]	Option Cancellation Agreement, by and between the Company and Timothy Ruane, dated December 27, 2012.
21.1	List of Subsidiaries.
23.1	Consent of Burr Pilger Mayer, Inc., Independent Registered Public Accounting Firm.
24.1	Reference is hereby made to the Power of Attorney included on the signature page to this Annual Report on Form 10-K.
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following materials from InSite Vision, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2012, formatted in XBRL (Extensible Business Reporting Language): (i) the Consolidated Statements of Income, (ii) the Consolidated Balance Sheets, (iii) the Consolidated Statements of Stockholders' Deficit, (iv) the Consolidated Statements of Cash Flows, and (v) Notes to Consolidated Financial Statements.

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 December 16, 2011.
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 the Company's Annual Report on Form 10-K for the year ended December 31, 1996.
13. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001.
14. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2007.
15. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012
16. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2008.
17. Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2008.
18. Incorporated by reference to an exhibit in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on April 29, 2009.
19. Incorporated by reference to an exhibit in the Company's Amendment No. 1 to Annual Report on Form 10-K filed with the Securities and Exchange Commission on April 30, 2009.
20. Incorporated by reference to an exhibit in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 30, 2010.
21. Incorporated by reference to an exhibit in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 18, 2011.
22. Incorporated by reference to an exhibit in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 27, 2012.

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

HH Management contract or compensatory plan.

Exhibit 21.1

Subsidiaries of InSite Vision Incorporated

Name	Place of Incorporation
Azithromycin Royalty Sub, LLC	Delaware
Ophthalmic Solutions, Inc.	Delaware
InSite Vision, Ltd.	United Kingdom

Exhibit 23.1

Consent of Burr Pilger Mayer, Inc., Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements on Form S-1 (No. 333-176057), Forms S-3 (No. 333-38266, No. 333-142049, No. 36673, 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. 333-186572, No. 333-149832, No. 333-171942, No. 333-179038, 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 report dated March 26, 2013, with respect to the consolidated financial statements which appear in this Form 10-K.

/s/ Burr Pilger Mayer, Inc.

San Francisco, California
March 26, 2013

EXHIBIT 31.1

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

I, Timothy Ruane, 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 26, 2013

/s/ TIMOTHY RUANE

Timothy Ruane
Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

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

I, Louis 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 26, 2013

/s/ LOUIS DRAPEAU

Louis Drapeau
Chief Financial Officer
(Principal Financial Officer)

EXHIBIT 32.1

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

I, Timothy Ruane, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of InSite Vision Incorporated on Form 10-K for the annual period ended December 31, 2012 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report of InSite Vision Incorporated on Form 10-K fairly presents, in all material respects, the financial condition and results of operations of InSite Vision Incorporated.

By: /s/ TIMOTHY RUANE
Name: **Timothy Ruane**
Title: **Chief Executive Officer**
(Principal Executive Officer)
Date: **March 26, 2013**

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

I, Louis Drapeau, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of InSite Vision Incorporated on Form 10-K for the annual period ended December 31, 2012 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report of InSite Vision Incorporated on Form 10-K fairly presents, in all material respects, the financial condition and results of operations of InSite Vision Incorporated.

By: /s/ LOUIS DRAPEAU
Name: **Louis Drapeau**
Title: **Chief Financial Officer**
(Principal Financial Officer)
Date: **March 26, 2013**

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Corporate and Stockholder Information

Executive Team

Timothy Ruane
Chief Executive Officer

Louis Drapeau
Vice President, Chief Financial Officer

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

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

Surendra Patel
Vice President, Operations
and Quality

Board of Directors

Timothy McInerney,
Chairman of the Board
Partner, Riverbank Capital Securities

Brian Levy O.D. M.Sc.
Chief Medical Officer,
Aerie Pharmaceuticals, Inc.

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

Timothy Ruane
Chief Executive Officer

Craig Tooman
Chief Executive Officer,
Avanzar Medical, Inc.

Anthony J. Yost
Chief Commercial Officer,
Prometheus Laboratories, Inc.

Corporate Headquarters

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

Corporate Counsel

Jones Day
Palo Alto, California

Independent Auditors

Burr Pilger Mayer, Inc.
San Francisco, California

Transfer Agent and Registrar

American Stock Transfer
& Trust Company, LLC
6201 15th Avenue
Brooklyn, NY 11219
tel: 800.937.5449
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 closing sale price for its common stock was $0.31 on April 8, 2013.

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 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 numerous 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 other reports filed with the Securities and Exchange Commission. 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.

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