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, 2006

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:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.01 par value per share	American Stock Exchange

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

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

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

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

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

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

Large Accelerated Filer ☐ Accelerated Filer ☒ Non-accelerated Filer ☐

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, 2006 was approximately $124,602,189 (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 15, 2007: 93,472,187.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement in connection with the 2007 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein.

ANNUAL REPORT ON FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2006

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

PART I

Item 1. Business

THE COMPANY

We are an ophthalmic product development company focused on ophthalmic pharmaceutical products based on our proprietary DuraSite® eyedrop-based drug delivery technology, as well as the development of genetically-based technologies for the diagnosis, prognosis and management of glaucoma.

With our existing resources, we are focusing our research and development and commercial out-licensing efforts on the following:

- AzaSite™ (ISV-401), a DuraSite formulation of azithromycin, a broad spectrum antibiotic; and
- AzaSite Plus™ (ISV-502), a DuraSite formulation of azithromycin and a steroid for inflammation and infection.

AzaSite (ISV-401). To treat bacterial conjunctivitis and other infections of the outer eye we have developed a topical ophthalmic formulation (AzaSite) of the antibiotic azithromycin, an antibiotic with a broad spectrum of activity that is widely used to treat respiratory and other infections in its oral and parenteral forms. We believe that the key advantages of AzaSite may include significantly fewer doses per day, enabled by the high and persistent levels of azithromycin achieved by our formulation in the tissues of the eye and its wide spectrum of activity. Product safety and efficacy have been shown, respectively, in Phase 1, Phase 2 and Phase 3 clinical trials.

In July 2004, we initiated two pivotal Phase 3 clinical trials for AzaSite which were conducted both in the United States and in selected Latin American countries. One of the Phase 3 clinical trials was a multi-center study in which patients in one arm were dosed with a 1% AzaSite formulation and the patients in the second arm were dosed with a 0.3% formulation of the antibiotic tobramycin. In November 2005, we announced that upon completion of enrollment this study included a total of 747 patients 1 year or older, of which 316 were confirmed positive for acute bacterial conjunctivitis in at least one eye. The results of this Phase 3 study indicated that AzaSite demonstrated a clinical resolution rate of 80% as compared to 78% for tobramycin. This result shows that the clinical resolution rate of AzaSite is equivalent to tobramycin, the primary efficacy endpoint of the study, according to statistical criteria which were previously agreed to by the U.S. Food and Drug Administration, or FDA. The bacterial eradication rate was also equivalent for both groups.

The other Phase 3 clinical trial was a multi-center study in which patients in one arm were dosed with a 1% AzaSite formulation and patients in the second arm were dosed with a placebo. In January 2006, we completed enrollment in this study of 685 patients, of which 279 were confirmed positive for acute bacterial conjunctivitis in at least one eye. In March 2006, we announced that the results of this study showed that the AzaSite formulation was more effective than the placebo in clinical resolution ($p < 0.03$), which includes reduction in discharge and redness, and bacterial eradication ($p < 0.001$).

In June 2006, we completed the compilation and assembly of an AzaSite New Drug Application, or NDA, and submitted the documentation to the FDA. Based on the FDA's Prescription Drug User Fee Act, or PDUFA, we anticipate a ruling by the FDA on the potential approval of AzaSite by the end of April 2007.

On February 15, 2007, we entered into a worldwide, exclusive, royalty bearing licensing agreement with Pfizer Inc. and Pfizer Products, Inc., or collectively 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, or the Pfizer License. Under the Pfizer License, we are required to pay Pfizer a single digit royalty based on net sales of the licensed products and to use reasonable commercial efforts to seek regulatory approval for and market licensed products.

On February 15, 2007, we entered into a license agreement, or the Inspire License, with Inspire Pharmaceuticals, Inc., or Inspire, under which we licensed to Inspire exclusive development and commercialization rights, under our AzaSite™ patent rights and certain know-how, for topical anti-infective products containing azithromycin as the sole active ingredient for human ocular or ophthalmic indications, or the Subject Products, in the United States and Canada and their respective territories, or the Territory. Inspire is a biopharmaceutical company dedicated to discovering, developing and commercializing prescription pharmaceutical products focused in the ophthalmic and respiratory/allergy therapeutic areas. The Inspire License also provides for nonexclusive licenses under our DuraSite® patent rights, container patent rights, certain patent rights licensed from Columbia Laboratories, Inc, or the Columbia patent rights, and certain know-how in the same field of use as described above. We also granted Inspire an exclusive sublicense under the Pfizer patent rights that we have licensed under the Pfizer License discussed above. Inspire has the right to grant sublicenses under the terms of the Inspire License.

Upon the closing of the Inspire License, Inspire paid us an upfront license fee of $13 million and is obligated to pay us an additional $19 million upon regulatory approval and the approval of an acceptable label for any Subject Product by the U.S. FDA. Inspire will also pay a royalty on net sales of any Subject Product in the Territory, if approved by regulatory authorities. The royalty rate will be 20% of net sales of any Subject Product in the first two years of commercialization and 25% thereafter. Inspire is obligated to pay us royalties under the Inspire License for the longer of (i) eleven years from the launch of the first product and (ii) the period during which a valid claim under a patent licensed from us covers a Subject Product. For five years after the first year of commercial sale, Inspire is required to pay us the greater of the running royalty discussed above and certain tiered minimum royalties. The royalties discussed above are subject to certain reductions in the event of patent invalidity, generic competition, uncured material breach or in the event that Inspire is required to pay license fees to third parties for the continued use of such Subject Product. Such reductions are cumulative but will in no event fall below a low single digit royalty based on applicable net sales. There are certain permitted offsets against both running royalties and minimum royalties which are not subject to a floor amount. In the event of a substantial reduction in our royalty rate, our royalties under the Inspire License could fall below our royalty obligations to Pfizer and other parties related to the products licensed to Inspire.

Under the Inspire License, we are responsible for obtaining regulatory approval of AzaSite™ in each country in the Territory. We also granted Inspire an exclusive option to negotiate with us for a license agreement for AzaSite Plus™, a combination antibiotic/corticosteroid product formulated with DuraSite® technology.

We also entered into a trademark license agreement with Inspire on February 15, 2007 under which we granted to Inspire an exclusive license to the AzaSite™ trademark and domain name and a nonexclusive license to the DuraSite® trademark in connection with the commercialization of Subject Products in the Territory under the terms of the Inspire License.

We also entered into a supply agreement, or the Supply Agreement, with Inspire on February 15, 2007 for the active pharmaceutical ingredient azithromycin. We had previously entered into a third party supply agreement for the production of such active ingredient. Under the Supply Agreement, we agreed to supply Inspire's requirements of such active ingredient, pursuant to certain forecasting and ordering procedures.

Cardinal Health PTS, L.L.C., or Cardinal Health has manufactured the AzaSite clinical trial supplies used in our two Phase 3 bacterial conjunctivitis clinical trials, and also the registration batches submitted with the AzaSite NDA. We believe this contract manufacturing facility is ready for inspection in relation to our NDA submission. As part of the Inspire License we are required to assist Inspire to enter into a manufacturing supply agreement consistent with the agreement we entered into with Cardinal Health in September 2005 for the production of AzaSite for the United States if the NDA is approved by the FDA.

AzaSite Plus (ISV-502). The expansion of our AzaSite product franchise will begin with the development of a combination of azithromycin with an anti-inflammatory steroid for the treatment of blepharitis, an infection of the eyelid and one of the most common eye problems in older adults, as well as other ophthalmic infections. In 2006, we completed our preclinical development of this combination product candidate, filed an Investigational New Drug Application, or IND, with the FDA and conducted a Phase 1 clinical trial.

The Phase 1 clinical study was intended to evaluate both the safety and tolerability of the AzaSite Plus formulation in normal volunteers. The trial enrolled 46 subjects with ages ranging from 19 to 67 years. Trial participants received eye drops of either placebo or AzaSite Plus two times daily for 14 days. Demographic characteristics were evenly distributed across treatment groups.

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

Business Strategy. Our business strategy is to license promising product candidates and technologies from academic institutions and other companies to which to apply our ophthalmic formulation expertise, to conduct preclinical and clinical testing, if necessary, to partner with pharmaceutical companies to complete clinical development and regulatory filings as needed and to manufacture and market our products. We also have internally developed DuraSite-based product candidates using either non-proprietary drugs or compounds developed by others for non-ophthalmic indications. As with in-licensed product candidates, we either have or plan to partner with pharmaceutical companies to complete clinical development and commercialize our own product candidates.

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

Ophthalmic Pharmaceutical Market

As the risk of most ophthalmic diseases increases with age, the U.S. ophthalmic market is projected to outpace the growth of the worldwide ophthalmic market due to the aging "baby-boomer" population. The prevalence of eye disease increases disproportionately with age and is ten times greater in persons over the age of 65. The U.S. Census Bureau projects that the U.S. population over age 65 will increase from 34 million in 1997 to approximately 69 million by the year 2030. We believe that this aging of the U.S. population and similar trends in other developed countries will lead to increased demand for new ophthalmic products.

In addition to changing demographics, we believe that emerging medical technologies, such as genetics, will assist eye care physicians in understanding the patho-physiology of serious eye diseases like glaucoma, which will allow the identification and treatment of ocular disease at an earlier stage.

New drug formulations and delivery methods are also being developed to deliver lower concentrations of drugs over an extended period of time. Whether these enhanced delivery technologies are focused on age-related macular degeneration (AMD) or bacterial conjunctivitis (pink eye), the emergence of these products will lead to increased patient compliance and fewer complications due to inconsistent drug administration.

There are approximately 119 million Americans who are over 40, which is the age at which serious eye diseases typically become a problem. Some 35 million are already affected by the four most prevalent: age-related macular degeneration, diabetic retinopathy, glaucoma, and cataracts. With the leading edge of the baby-boomer generation approaching 60, the number of eye-disease sufferers is expected to increase dramatically, topping 50 million or more over the next 15 years in the United States alone.

Our lead product is AzaSite, which targets infections of the eye and is part of the ophthalmic anti-infective or antibiotic market. The global ophthalmic anti-infective market was approximately 1.5 billion dollars in 2006 according to a study conducted by Navigant Consulting. The market is comprised of two separate product segments:

- Ocular antibiotic products
- Ocular antibiotic/steroid combination products

Both the antibiotic and combination antibiotic/steroid markets are expected to experience healthy growth in the future. New product developments, growth of less-industrialized nations, and an expanding elderly population are factors expected to support continued growth.

Products and Product Candidates

The following table summarizes the current status of our principal products and product candidates. A more detailed description of each product and product candidate follows the table. There can be no assurance that any of the listed products or product candidates will progress beyond its current state of development, receive necessary regulatory approval or be successfully marketed.

Principal Products and Product Candidates

Product	Indications	Anticipated Benefits	Status(1)
Active Programs			
Anti-infectives			
AzaSite (ISV-401)	Bacterial infection including ophthalmia neonatorum	Broad spectrum antibiotic with reduced dosing frequency	NDA filed
AzaSite Plus (ISV-502)	Blepharitis and other ophthalmic infections	Broad spectrum antibiotic with reduced dosing frequency	Phase 1 completed
AzaSite Otic (ISV-016)	Otic infections	Broad spectrum antibiotic with reduced dosing frequency	Preclinical
Other Topical Product Candidates and Marketed Product			
ISV-205	Inflammation and analgesia	Reduced dosing frequency	Preclinical
AquaSite	Dry eye	Reduced dosing frequency and extended duration of action	Marketed (OTC)
Glaucoma Genetics			
OcuGene – Glaucoma Genetic Test	Glaucoma severity (TIGR gene)	Determine disease severity among glaucoma patients	Marketed
Inactive Programs			
Glaucoma Product Candidates			
ISV-205	Steroid-induced intraocular pressure elevation, glaucoma	Treat/prevent disease progression	Phase 2(b) completed
Retinal Device			
ISV-014	Retinal drug delivery device for potential treatment of diabetic retinopathy and macular degeneration	Non-surgical delivery of drugs to the retina	Research

1) All products except OcuGene, AquaSite and ISV-014 are expected to be prescription pharmaceuticals. As denoted in the table, "Preclinical" follows the research stage and indicates that a specific compound is being tested in preclinical studies in preparation for filing an investigational new drug application, or IND. For a description of preclinical trials, IND, Phase 1, Phase 2 and Phase 3 clinical trials and New Drug Application, or NDA, see "—Government Regulation."

Anti-infectives

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

Azithromycin has a broad spectrum of antibiotic activity and is widely used to treat respiratory and other infections in its oral and parenteral forms. AzaSite is an eye drop of 1% azithromycin formulated to deliver sufficient tissue concentrations over a 5-day dosing period using our proprietary DuraSite technology. The eyedrop is designed to enable superior bactericidal activity against common ocular pathogens and pseudomonas. We believe the key advantages of AzaSite may include significantly fewer doses per day, the high and persistent levels of azithromycin achieved in the tissues of the eye and its wide spectrum of activity. Phase 1, 2 and 3 studies have shown that AzaSite is well tolerated and efficacious.

AzaSite has been formulated to meet the regulatory requirements for the United States and most other countries. Our marketing emphasis, through our partner Inspire, will focus on pediatricians, general practitioners, optometrists, and ophthalmologists. Pediatricians and general practice physicians write more than 65% of total prescriptions for ophthalmic antibiotics. We expect that if and when it is approved and commercialized, AzaSite will be positioned to compete favorably with the newer 4th generation fluoroquinolones for antibacterial coverage. Further, AzaSite possesses the advantage of reduced dosing frequency that, we believe, may ultimately increase patient compliance and reduce the likelihood of the development of bacterial resistance.

AzaSite Plus (ISV-502). Our first effort toward the expansion of our product candidate AzaSite into a larger franchise is the development of a combination of AzaSite with an anti-inflammatory steroid for the treatment of blepharitis, an infection of the eyelid and one of the most common eye problems in older adults, as well as other ophthalmic infections. In 2006, we completed our preclinical development of this combination product candidate, filed an IND with the FDA and conducted a Phase 1 clinical trial.

AzaSite Otic (ISV-016). In a continued effort to expand the AzaSite franchise we have begun to evaluate the use of the AzaSite Plus combination as a treatment for ear infections. This product candidate is currently in preclinical development and we anticipate pursuing it more actively if and when personnel and financial resources become available.

Other Topical Product Candidates and Marketed Product

AquaSite. The first product utilizing our DuraSite technology was introduced to the OTC market in the United States in October 1992 by CIBA Vision. We receive a royalty on sales of AquaSite by CIBA Vision. The product contains the DuraSite formulation and demulcents for the symptomatic treatment of dry eye. In March 1999, we licensed AquaSite to Global Damon Pharm, a Korean company. The license is royalty-bearing, has a term of 10 years and is exclusive in the Republic of Korea. In August 1999, we entered into a ten year royalty-bearing exclusive license with SSP Co., Ltd, or SSP, for the sale and distribution of AquaSite in Japan.

Inflammation and Glaucoma Product Candidates

ISV-205. Our ISV-205 product candidate contains the drug diclofenac formulated in the DuraSite sustained-release delivery vehicle. Diclofenac is a non-steroidal anti-inflammatory drug or NSAID currently used to treat ocular inflammation. NSAIDs can block steroid-induced intraocular pressure, or IOP, elevation by inhibiting the production of the trabecular meshwork glucocorticoid response, or TIGR, protein that appears to affect the fluid balance in the eye. Our ISV-205 product candidate delivers concentrations of diclofenac to the eye that have been shown in cell culture systems to inhibit the production of the TIGR protein.

We successfully completed a Phase 2a clinical study in 1999 that evaluated the efficacy of two concentrations of diclofenac. Analysis of the data from this study indicates that ISV-205 was safe and associated with a 75% reduction in the number of subjects with clinically significant IOP elevation following steroid use.

In 2001 we completed a Phase 2b clinical study that was conducted in 233 subjects with ocular hypertension. Genetic information was collected on the subjects using our ISV-900 technology and the subjects were dosed twice daily for six months with ISV-205. Our ISV-900 technology detected the TIGR mt-1 or mt-11 sequence variations in approximately 70% of the ocular hypertensive patients participating in the study. In patients with the TIGR sequence variations, a 0.1% formulation of our ISV-205 product candidate was significantly more effective than placebo in lowering IOP ($p = 0.008$). These effects were not seen to the same extent in patients without the TIGR mutations. ISV-205 was similar to placebo in ocular safety and comfort in all patients. Only with the infusion of additional financial resources will we plan further clinical studies of ISV-205. To the extent that we initiate further studies, we cannot assure you that similar clinical results will be achieved.

Other potential indications for ISV-205 may include glaucoma prevention, analgesia and anti-inflammatory indications. Co-exclusive rights, in the United States, to develop, manufacture, use and sell ISV-205 to treat non-glaucoma indications of inflammation and analgesia, were licensed to CIBA Vision in May 1996. See "Business — Collaborative, Licensing and Service Agreements."

Glaucoma Genetics

According to the Glaucoma Research Foundation, glaucoma is the leading cause of preventable blindness in the United States, affecting an estimated two to three million people. The most prevalent form of glaucoma in adults is primary open angle glaucoma, or POAG.

Often called the "sneak thief of sight" because of its lack of symptoms, glaucoma is believed to result when the flow of fluid through the eye is impaired. This may lead to elevated IOP, which increases pressure on the optic nerve and can cause irreversible vision loss if left untreated. However, one form of glaucoma, normal or low-tension glaucoma, is associated with individuals who have normal eye pressure. It is estimated that one-third of U.S. glaucoma patients and three-quarters of glaucoma patients in Japan have this form of the disease, based on a study conducted by Dr. Yoshiaki Kitazawa in Japan. These patients cannot be identified with standard glaucoma screening tests that only measure a patient's eye pressure and these patients usually incur visual field loss before they are diagnosed.

OcuGene. Current glaucoma tests are often unable to detect the disease before substantial damage to the optic nerve has occurred. Gene-based tests may make it possible to identify patients at risk and initiate treatment before permanent optic nerve damage and vision loss occurs. OcuGene has been developed to help determine the potential severity of a patient's glaucoma, and the product was commercially launched at the end of 2001. However, development of additional clinical data will be necessary to support the market utility of this product. We do not anticipate pursuing additional clinical studies and other marketing activities for this product until at least such time as we obtain substantial additional funding. We currently hold licenses to patents issued on the TIGR cDNA, TIGR antibodies, and methods for the diagnosis of glaucoma using the TIGR technology.

In December 2002, we entered into an agreement with Società Industria Farmaceutica Italiana, or SIFI, that grants SIFI the exclusive right to manufacture/perform, distribute and market OcuGene in Italy for eight years. SIFI introduced the OcuGene test at two Italian ophthalmic meetings in late 2003, and is currently conducting additional clinical studies to evaluate the technology in the Italian population.

Retinal Device

Ophthalmic conditions that involve retinal damage include macular degeneration, which according to the American Macular Degeneration Foundation affects 10 million or more people in the United States, and diabetic retinopathy, a common side effect of diabetes. According to the National Diabetes Education Foundation, approximately 16 million people in the United States are diabetics. Both macular degeneration and diabetic retinopathy can lead to irreversible vision loss and blindness. Current treatment of retinal diseases, including diabetic retinopathy and macular degeneration, generally involves surgery, laser, photo-dynamic therapies and intravitreal drug injection, each of which can lead to loss of vision, retinal detachment, infection and may not slow the progression of the disease.

Retinal Delivery Device. ISV-014 is one of our technology platforms and consists of a device for the controlled, non-surgical delivery of ophthalmic drugs to the retina and surrounding tissues. During 2002, we continued to enhance the device and performed in vivo experiments delivering products with a variety of molecular sizes to retinal tissues. The combination of this device technology with viral or small molecule drug platforms may permit long-term delivery of therapeutic agents to treat several retinal diseases, including diabetic retinopathy and macular degeneration, most of which cannot be effectively treated at the present time.

The ISV-014 device consists of a handle with a distal platform that is placed against the surface of the eye. A small needle connected to a drug reservoir is extended from the platform into the tissues of the eye. Once in place, a metering mechanism controls the amount and rate that the drug is injected into the tissue. This produces a highly localized depot of drug inside the ocular tissues. By controlling both the distance and direction that the needle protrudes, the device greatly reduces the chance that the needle will penetrate through the sclera of the eye into the underlying tissues, which are easily damaged. We have filed two patent applications related to the device. In the United States two patents have been issued on the design and two patents have been issued on the method of use. We have placed further development of the device on hold and are pursuing the licensing of this technology to third parties.

Collaborative, Licensing and Service Agreements

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

Pfizer Inc. and Pfizer Products, Inc. On February 15, 2007, we entered into a worldwide, exclusive, royalty-bearing licensing agreement with Pfizer, under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus. Under the Pfizer License, we are required to pay Pfizer a single digit royalty based on net sales of the licensed products and to use reasonable commercial efforts to seek regulatory approval for and market licensed products. We have the right to grant sublicenses, subject to Pfizer's prior approval which under the Pfizer License shall not be unreasonably withheld. On February 15, 2007, with Pfizer's approval, we granted a sublicense to Inspire as described below.

Inspire Pharmaceuticals, Inc. On February 15, 2007, we entered into the Inspire License with Inspire, under which we licensed to Inspire exclusive development and commercialization rights, under our AzaSite™ patent rights and certain know-how, for topical anti-infective products containing azithromycin as the sole active ingredient for human ocular or ophthalmic indications, or each a Subject Product, in the United States and Canada and their respective territories, or the Territory. The Inspire License also provides for nonexclusive licenses under our DuraSite® patent rights, container patent rights, Columbia patent rights and certain know-how in the same field of use as described above. We also granted Inspire an exclusive sublicense under the Pfizer patent rights that we have licensed under the Pfizer License discussed above. Inspire has the right to grant sublicenses under the terms of the Inspire License.

Upon the closing of the Inspire License, Inspire paid us an upfront license fee of $13 million and is obligated to pay us an additional $19 million upon regulatory approval and the approval of an acceptable label for any Subject Product by the U.S. FDA. Inspire will also pay us a royalty on net sales of any Subject Product in the Territory, if approved by regulatory authorities. The royalty rate will be 20% of net sales of any Subject Product in the first two years of commercialization and 25% thereafter. Inspire is obligated to pay us royalties under the Inspire License for the longer of (i) eleven years from the launch of the first product, and (ii) the period during which a valid claim under a patent licensed from us covers a Subject Product. For five years after the first year of commercial sale, Inspire is required to pay us the greater of the running royalty discussed above or certain tiered minimum royalties. The royalties discussed above are subject to certain reductions in the event of patent invalidity, generic competition, uncured material breach or in the event that Inspire is required to pay license fees to third parties for the continued use of such Subject Product. Such reductions are cumulative but will in no event fall below a low single digit royalty based on applicable net sales. There are certain permitted offsets against both running royalties and minimum royalties which are not subject to a floor amount.

Under the Inspire License, we are responsible for obtaining regulatory approval of AzaSite™ in each country in the Territory. No more than 25 days after obtaining regulatory approval for each country in the Territory, we will be

responsible for transferring regulatory documentation regarding AzaSite™, including the New Drug Application and Canadian equivalent, to Inspire. Thereafter, Inspire will be responsible for all regulatory obligations and strategies relating to the further development and commercialization of products in each country in the Territory. Inspire will also be responsible for all commercialization in the Territory.

Under the Inspire License we also granted Inspire an exclusive option to negotiate with us for a license agreement for AzaSite Plus™, a combination antibiotic/corticosteroid product formulated with DuraSite® technology. If we enter into a definitive agreement with Inspire with respect to AzaSite™ Plus or if we publicly announces that we are no longer pursuing the development of AzaSite™ Plus, then the AzaSite™ trademark, the AzaSite™ domain names and the AzaSite™ Plus trademark, including all goodwill associated therewith, will be assigned to Inspire in the Territory.

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

We also entered into a trademark license agreement with Inspire on February 15, 2007 under which we granted to Inspire an exclusive license to the AzaSite™ trademark and domain name and a nonexclusive license to the DuraSite® trademark in connection with the commercialization of Subject Products in the Territory under the terms of the Inspire License.

We also entered into a supply agreement, or the Supply Agreement, with Inspire on February 15, 2007 for the active pharmaceutical ingredient azithromycin. We had previously entered into a third party supply agreement for the production of such active ingredient. Under the Supply Agreement, we agreed to supply Inspire's requirements of such active ingredient, pursuant to certain forecasting and ordering procedures. The initial term of the Supply Agreement is until 2012, subject to customary termination provisions, such as termination for material breach. Either party may terminate the Supply Agreement upon 180 days notice to the other party. In addition, Inspire may also terminate the Supply Agreement if our third-party supplier moves the location at which the active ingredient is manufactured. After 2012, the Supply Agreement automatically renews for successive three-year periods unless terminated pursuant to the foregoing termination provisions. If we are in breach of our supply obligations under the Supply Agreement, Inspire is permitted to qualify a second source supplier, at our expense, and obtain the active ingredient from such second source. We are obligated under the Supply Agreement to maintain a minimum quantity of the active ingredient in inventory for Inspire's use in manufacturing such products and to maintain the quality agreement negotiated with its supplier. The Supply Agreement also contains certain provisions regarding the rights and responsibilities of the parties with respect to manufacturing specifications, delivery arrangements, quality assurance, regulatory compliance, product recall, and indemnification, as well as certain other customary matters.

Cardinal Health PTS, L.L.C. In September 2005, we entered into a commercial manufacturing supply agreement with Cardinal Health for the manufacture of AzaSite commercial units. The agreement has a term of four years subsequent to the approval by the FDA of Cardinal Health as a manufacturer of AzaSite. Payments under the contract will be dependent upon rolling production forecasts we will provide to Cardinal Health and are subject to certain minimum purchase commitments which escalate over the term of the contract.

Bausch and Lomb Incorporated. On December 30, 2003, we completed the sale of our drug candidate ISV-403 for the treatment of ocular infections to Bausch & Lomb Incorporated, or Bausch & Lomb, pursuant to an ISV-403 Purchase Agreement dated December 19, 2003, or the Purchase Agreement and a License Agreement dated December 30, 2003, or the License Agreement, and collectively, the Asset Sale.

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

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

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

SIFI In December 2002, we entered into an exclusive distribution agreement with SIFI for OcuGene in Italy. The distribution agreement grants SIFI the right to manufacture, directly or indirectly, distribute, perform, market, sell and promote our OcuGene glaucoma genetic test in Italy. Over the initial eight-year term of the agreement SIFI will pay us a fee for each test conducted. The agreement may be extended by SIFI for additional two year periods if certain sales targets are met during the initial and extension periods.

Quest Diagnostics Incorporated. In November 2002, we extended an exclusive laboratory service agreement with Quest Diagnostics Incorporated, or Quest, for our OcuGene test in the United States. Under this agreement, we pay Quest for each OcuGene test that they perform.

CIBA Vision Ophthalmics. In October 1991, we entered into license agreements with CIBA Vision which granted CIBA Vision certain co-exclusive rights to manufacture, have manufactured, use and sell, in the United States and Canada fluorometholone and tear replenishment products utilizing the DuraSite technology, ISV-205 for non-glaucoma indications, and ToPreSite®, a product candidate for ocular inflammation/infection (the development of which is currently not being pursued by us or Ciba Vision).

UC Regents. In March 1993, we entered into a license agreement with the UC Regents granting us certain exclusive rights for the development of ISV-205 and, in August 1994, we entered into another license agreement with the UC Regents granting us certain exclusive rights for the use of a nucleic acid sequence that codes for a protein associated with glaucoma. Under both agreements, we paid initial licensing fees, share sub-licensing fees we receive, if any, and will make royalty payments to the UC Regents on future product sales, if any.

Columbia Laboratories, Inc. In February 1992, we entered into a cross-license agreement with Columbia in which Columbia licensed to us certain exclusive rights to a polymer technology upon which DuraSite is based. This license permits us to make, use and sell products using such polymer technology for non-veterinary ophthalmic indications in the over-the-counter and prescription markets in North America and East Asia, collectively Columbia Territory, and in the prescription market in countries outside the Columbia Territory. In exchange, we granted Columbia a license with certain exclusive rights to sublicense and use certain DuraSite technology in the over-the-counter market outside the Columbia Territory. In addition, we also granted Columbia a license with certain exclusive rights to DuraSite technology in the veterinary field. Under certain circumstances, certain of the licenses in the Columbia Agreement become non-exclusive. Subject to certain rights of early termination, the Columbia Agreement continues in effect until the expiration of all patents covered by the DuraSite technology to which Columbia has certain rights.

SSP. In April 2001, we entered into a royalty-bearing license agreement with SSP for two fourth-generation fluoroquinolones, one of which is the active ingredient in ISV-403. We have worldwide development and marketing rights except for Japan, which were retained by SSP, and will share the rights with SSP in Asia. We subsequently assigned our rights under this agreement for the active ingredient in ISV-403 to Bausch & Lomb.

Other. As part of our basic strategy, we continually pursue agreements with other companies, universities and research institutions concerning the licensing of 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, though 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 important to the development of our business. Additionally, we assist UC Regents in filing patent applications seeking to protect inventions that are the subject of our agreements with them. 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, including two U.S. patents owned by Columbia and exclusively licensed to us in the field of human ophthalmic applications. In addition, we have filed a number of patent applications in the United States relating to our DuraSite technology with delivery tips and drug compounds. Of these applications, seven U.S. patents have been issued. Of the patent applications we have licensed from the UC Regents, twelve U.S. patents have been issued. We have four U.S. patents on our retinal drug delivery device that have been issued. Three U.S. patents have been issued related to our antibiotic programs with three applications pending. Several other patent applications by us and by the UC Regents, relating to the foregoing and other aspects of our business and potential business are also pending. Foreign counterparts of our patents as well as those we have licensed from others have been filed in many countries.

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

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

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

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

Research and Development

On December 31, 2006, our research and development staff numbered 32 people, of whom 6 have Ph.D.s. In 2006, our research and development expenses were $8.9 million. In 2005, our research and development expenses were $10.7 million. In 2004, our research and development expenses, including third-party research we sponsored, were $6.8 million, including the expenses related to contract research activities for which we received $537,000 from Bausch & Lomb.

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 implementing 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, as stated above, we have no large-scale manufacturing capacity and we rely on third parties for supplies and materials necessary for all of our Phase 3 clinical trials. If we should encounter delays or difficulties in establishing and maintaining our relationship with qualified manufacturers to produce, package and distribute our finished products, then clinical trials, regulatory filings, market introduction and subsequent sales of such products would be adversely affected.

We have entered into a manufacturing supply agreement for commercial units of our AzaSite product candidate with Cardinal Health. Cardinal Health was the manufacturer of our AzaSite Phase 3 clinical trial supplies and registration batches to validate their production line for commercial scale batches and will manufacture the required validation batches for FDA review. Cardinal Health's facility and the line that may be used to produce the AzaSite units will be subject to inspection by the FDA prior to the approval of the related NDA that we filed in 2006. While we believe Cardinal Health will be prepared for the inspections, they could encounter delays or difficulties in preparing for, or during, the inspection which would adversely impact our potential market introduction and subsequent sales of AzaSite.

We have entered into a licensing agreement with Inspire under which they will be responsible for the manufacture of AzaSite for the United States and Canada if it is approved by the related regulatory agencies. As part of the license we have agreed to assist in the transition of our manufacturing supply agreement with Cardinal to Inspire. If Inspire encounters delays or difficulties in the transfer or in the future with maintaining their relationship with Cardinal or with establishing an arrangement with another qualified manufacturer, subsequent sales of AzaSite would be adversely affected.

Marketing and Sales

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

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

Our current collaborators include:

Inspire. In February 2007, we entered into an exclusive agreement with Inspire under which Inspire will be responsible for all sales and marketing associated with AzaSite and the other subject products under the Inspire License in the United States and Canada, if approved by the appropriate regulatory authorities. We received an upfront licensing fee and are entitled to a milestone payment if AzaSite is approved by the FDA and to royalties based on net sales of the subject products, if any. Inspire currently promotes to a select number of eye care professionals and allergists using 64 territory managers. Inspire also has a marketing team and a training and operations team to support its commercialization effort. Inspire's small, specialty sales and marketing organization focuses its promotional efforts on ophthalmologists, optometrists and allergists but upon an approval of AzaSite, will expand to select high prescribing pediatricians and primary care physicians. Inspire has publicly disclosed that if AzaSite receives regulatory approval, Inspire expects to increase its sales force to a total of approximately 98 representatives who will call on targeted specialists and selected pediatricians and primary care providers.

CIBA Vision. In 1991, we entered into a co-exclusive rights agreement with CIBA Vision under which CIBA Vision obtained the right to market the AquaSite product in the United States and Canada. Additionally, in May 1996, we granted CIBA Vision a co-exclusive U.S. license for ISV-205 for non-glaucoma indications, and co-exclusive marketing rights within the United States to sell and use ToPreSite, a product candidate that currently is not being pursued. CIBA Vision is using our trademark, under license, for AquaSite dry eye treatment and our patents are identified on the AquaSite packaging. We received a one-time licensing fee and are entitled to royalties based on net sales of the products, if any.

SSP. In April 2001, we entered into an exclusive licensing agreement with SSP for two fluoroquinolone compounds, one of which is incorporated into ISV-403. We have exclusive marketing rights for the world except for Japan, which SSP retained, and shared rights with SSP in the rest of Asia. In December 2003 we assigned our rights under this agreement to the compound incorporated into ISV-403 to Bausch & Lomb.

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

SIFI. In December 2002, we entered into an exclusive licensing agreement with SIFI for OcuGene. SIFI has the exclusive right to manufacture/perform, distribute and market OcuGene in Italy. We provide SIFI with access to technical information related to OcuGene and provide them access to any marketing materials we develop with respect to OcuGene to aid them in their sales and distribution efforts.

Competition

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

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

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

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

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

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

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.

While the FDA currently does not regulate genetic tests, it has stated that it has the right to do so, and there can be no assurance that the FDA will not seek to regulate such tests in the future. If the FDA should require that genetic tests receive FDA approval prior to their use, there can be no assurance such approval would be received on a timely basis, if at all. The failure to receive such approval could require us to develop alternative testing methods, which could result in the delay of such tests reaching the market, if at all. Such a delay could materially harm our business.

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

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

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

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

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

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

The results of the preclinical studies and clinical studies are submitted to the FDA in the form of an NDA or PLA 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 PLA approval is the requirement that the prospective manufacturer’s quality control and manufacturing procedures conform to Good Manufacturing Practice, or GMP. Prior to approval, manufacturing facilities are subject to FDA and/or other

regulatory agency inspection to ensure compliance with GMP. Manufacturing facilities are subject to periodic regulatory inspection to ensure ongoing compliance.

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

Scientific and Business Advisors

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

Our advisors are as follows:

Name	Position
Mark Abelson, M.D.	Associate Clinical Professor of Ophthalmology, Department of Ophthalmology, Harvard Medical School
Chandler R. Dawson, M.D.	Emeritus Professor, Department of Ophthalmology, University of California, San Francisco
Syd Gilman, Ph.D.	Partner, Trident Rx Consultant Service
Ping H. Hsu, Ph.D.	Consultant, Biostatistics
David G. Hwang, M.D.	Professor of Clinical Ophthalmology, Co-Director, Cornea and Refractive Surgery Service, University of California, San Francisco School of Medicine
Henrick K. Kulmala, Ph.D.	Consultant, Pharmaceutical Development
Michael Marmor, M.D.	Professor, Department of Ophthalmology, Stanford University School of Medicine
James G. Shook, Ph.D.	President, Jim Shook Research, Inc.
Roger Vogel, M.D.	Co-Founder and Chief Medical Officer, Sirion Therapeutics, Inc.

Employees

As of December 31, 2006, we had 44 employees, 40 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

Our current cash will only fund our business until approximately the end of June 2007. We will need additional funding, either through achievement of a licensing milestone, equity or debt financings or partnering arrangements, that, if available, could be further dilutive to our stockholders and could negatively affect us and our stock price

Our independent auditors included an explanatory paragraph in their audit report to our consolidated financial statements for the fiscal year ended December 31, 2006 referring to our recurring operating losses and a substantial doubt about our ability to continue as a going concern.

We expect that our cash on hand (including cash received from the Inspire License in February 2007), together with a refund from the FDA relating to our NDA filing fee, anticipated cash flow from operations and current cash commitments to us will only enable us to continue operations until approximately the end of June 2007. At that point, or earlier if circumstances change from our current expectations, we will require substantial additional funding from the issuance of debt or equity securities, payments under existing collaboration agreements, asset sales

or other sources. We cannot assure you that additional funding will be available on a timely basis, or on reasonable terms, or at all.

If we are able to secure additional equity financing, the terms of any securities issued in connection with such financing may be superior to the rights of our then-current stockholders and could result in substantial dilution and could adversely affect the market price for our Common Stock. If we raise funds through the issuance of debt securities, such debt will likely be secured by a lien on all of our assets, including our intellectual property, will require us to make principal and interest payments in cash, securities or a combination thereof, and may subject us to restrictive covenants. Such equity or debt financings may also include the issuance of warrants exercisable for our Common Stock at a discount to the then current market price. In addition, the existence of the explanatory paragraph in the audit report may make it more difficult for us to raise additional financing, may adversely affect the terms of such financing and could prevent investors from purchasing our shares in the open market as certain investors may be restricted or precluded from investing in companies that have received this explanatory paragraph in an audit report. Further, the factors leading to the explanatory paragraph in the audit report may harm our ability to obtain additional funding and could make the terms of any such funding, if available, less favorable than might otherwise be the case. If we do not obtain additional financing when required, we would likely have to cease operations and liquidate our assets.

It is difficult to precisely predict our future capital requirements, and therefore the amount and timing of our future funding requirements depend upon many factors, including:

- the progress and results of the review of our NDA by the FDA;
- the progress and results of our preclinical and clinical testing;
- changes in, or termination of, our existing collaboration or licensing arrangements;
- the progress of our research and development programs;
- the initiation and outcome of possible future legal actions;
- whether we manufacture and market any of our other products ourselves;
- the time and cost involved in obtaining regulatory approvals;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- competing technological and market developments; and
- the purchase of additional capital equipment.

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

We are currently seeking FDA approval of an NDA for our AzaSite product and have completed Phase 1 clinical trials for our AzaSite Plus product candidate. We expect our cash on hand (including cash received from the Inspire License in February 2007), together with a refund from the FDA relating to our NDA filing fee, anticipated cash flow from operations and current cash commitments to us will only enable us to continue our operations until approximately the end of June 2007. While we have completed Phase 3 trials and submitted an NDA for AzaSite, the FDA may require further information or even additional clinical trials before granting final approval for AzaSite. Any delay or failure in the FDA approval process will delay our receipt of the milestone payment due under the Inspire License and will likely require us to obtain even further funding, and such delay or failure could make it much more difficult or expensive for us to obtain funding.

Human clinical trials for our product candidates are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time-consuming. We estimate that clinical trials of our product candidates, including AzaSite Plus, will take at least several years to complete. Furthermore, we could encounter problems that cause us to abandon or repeat clinical trials, further delaying or preventing the completion of such trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- unforeseen safety issues;
- determination of dosing issues;

- lack of effectiveness during clinical trials;
- slower than expected rates of patient recruitment;
- inability to monitor patients adequately during or after treatment; and
- inability or unwillingness of medical 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.

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 their results will support our product candidate claims. Even if pre-clinical testing and early clinical trials for a product candidate are successful, this does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and pre-clinical testing or meet our expectations. The clinical trial process may fail to demonstrate that our product candidates are safe for humans or effective for indicated uses. In addition, our clinical trials involve relatively small patient populations. Because of the small sample size, the results of these clinical trials may not be indicative of future results. Any such failure would likely cause us to abandon the product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay or preclude the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. For example, if the FDA determines that our current AzaSite Phase 3 trials did not produce sufficient evidence to obtain approval for the commercialization of AzaSite or the FDA refuses to accept or approve our AzaSite NDA for any other reason, our business would be significantly harmed as we have devoted a significant portion of our resources to this product candidate, at the expense of our other product candidates.

Our current financial situation may impede our ability to protect or enforce adequately our legal rights under our agreements and intellectual property

Our limited financial resources make it more difficult for us to enforce our intellectual property rights, through filing or maintaining our patents, taking legal action against those that may infringe on our proprietary rights, defending infringement and other patent claims against us, or otherwise. Our current financial situation may impede our ability to enforce our legal rights under various agreements we are currently a party to or may become a party to due to our inability to incur the costs associated with such enforcement. Our inability to adequately protect our legal and intellectual property rights may make us more vulnerable to infringement and could materially harm our business.

Our strategy for research, development and commercialization of our products requires us to enter into various arrangements with corporate and academic collaborators, licensors, licensees and others; furthermore, we are dependent on the diligent efforts and subsequent success of these outside parties in performing their responsibilities

Because of our reliance on third parties for the development, marketing and sale of our products, any revenues that we receive will be dependent on the efforts of these third parties, particularly Inspire. These partners may terminate their relationships with us and may not diligently or successfully market our products. In addition, marketing consultants and contract sales organizations that we may use in the future for other 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. We may not be able to conclude arrangements with other companies to support the commercialization of our products on acceptable terms, or at all. Moreover, our current financial condition may make us a less attractive partner to potential collaborators. Furthermore, our collaborators may pursue alternative technologies or develop alternative products either on their own or in collaboration with others, including our competitors, as a means for developing treatments for the diseases or disorders targeted by our collaborations.

Inspire's failure to successfully market and commercialize AzaSite would negatively impact our future revenues

In February 2007, we entered into the Inspire License where we exclusively licensed AzaSite to Inspire in the U.S. and Canada, or the Territory. If approved by the FDA in the United States or by the relevant regulatory authorities in Canada, Inspire will assume full control of all sales and marketing activities for AzaSite and other subject products. Accordingly, our royalty revenue on the net sales of AzaSite in the Territory will be entirely dependent on the actions, efforts and success of Inspire, over whom we have little or no control. The commercial success of AzaSite will depend on a number of factors, including:

- timing and scope of Inspire's launch and initiation of the commercialization of AzaSite in the United States and Canada;
- effectiveness and extent of Inspire's promotional, sales and marketing efforts;
- Inspire's ability to build, train and retain an effective sales force;
- Inspire's ability to successfully sell AzaSite to physicians and patients;
- Inspire's pricing decisions regarding AzaSite;
- our competitors' ability to market and sell current or future competing products;
- patient and physician satisfaction with existing alternative products;
- prevalence and severity of adverse side effects;
- the perceived efficacy of AzaSite relative to other available products;
- coverage and reimbursement under Medicare and other governmental or privately sponsored insurance plans;
- duration of market exclusivity of AzaSite;
- pricing and availability of alternative products, including generic or over-the-counter products; and
- shifts in the medical community to new treatment paradigms or standards of care.

Our license of AzaSite to Inspire may not be profitable for us

Under the Inspire License, if we receive regulatory approval for AzaSite or other subject products, Inspire will assume responsibility for all further commercialization activities, and we are entitled to receive royalties on the net sales of AzaSite and other subject products. Inspire's obligation to pay us royalties expires upon the later of eleven years from the launch of the first product, and the period during which a valid claim under one of our licensed patents covers a subject product, in each country in the Territory. While we are entitled to minimum royalty payments from Inspire for five years after the first year of a commercial sale, such minimum royalty payments will not be sufficient for us to cover our operating expenses, and we are dependent on Inspire's sales and marketing efforts for AzaSite in order for us to receive royalties in excess of these minimum amounts. In addition, our royalties are subject to a cumulative reduction in the event of patent invalidity, generic competition, uncured material breach or in the event that Inspire is required to pay license fees to third parties for the continued use of AzaSite. These cumulative reductions could result in us receiving a low single digit royalties on net sales of AzaSite and other subject products. Generic competition, over which we have little control, could also result in substantial reductions to our royalties under the Inspire License. In the event of generic competition, our royalty rate is reduced based on the economic impact to Inspire of such generic competition, potentially down to a low single digit royalty. We could ultimately lose money under the Inspire License in the event of a substantial reduction in our royalty rate combined with our royalty obligations to Pfizer and other parties related to the products licensed to Inspire.

If Inspire terminates the Inspire License as a result of our uncured material breach or insolvency, Inspire will have a 12-month wind-down period to sell products in inventory and the Inspire License will be terminated after the wind-down period. During such wind-down period our royalty payments would be subject to reduction and there is no guarantee that we could enter into a new license agreement with a third-party or otherwise commercialize AzaSite after the Inspire License is terminated.

Inspire has limited experience in sales and marketing of pharmaceutical products

If AzaSite receives regulatory approval in the United States and Canada, we will be dependent upon Inspire to market and sell AzaSite in those countries. Inspire has only recently established its sales force and did not have a sale organization prior to 2004. Inspire has disclosed that it has encountered difficulties and incurred substantial expenses in maintaining its sales force. Inspire may encounter similar or new problems in the future related to maintaining and growing its sales force that could have a negative impact on sales of AzaSite. We have no control over how Inspire manages and operates its sales force. In addition, there is no guarantee that Inspire can effectively compete with our competitors that currently have more extensive, more experienced and better funded marketing and sales operations.

Revenues in future periods could vary significantly and will be based on Inspire's financial reports

We will recognize revenue based on Inspire's net sales of AzaSite and other subject products as reported to us by Inspire. Inspire's net sales of AzaSite may vary quarter to quarter which would cause our royalty revenue to also vary. In addition our royalty revenues will be based upon Inspire's revenue recognition and other accounting policies over which we have no control. Inspire's filings with the SEC indicate that Inspire maintains disclosure controls and procedures in accordance with applicable laws, which are designed to provide reasonable assurance that the information required to be reported by Inspire in its Exchange Act filings is reported timely and in accordance with applicable laws, rules and regulations. However, if Inspire's reported revenue amounts or net sales reports were inaccurate, it could have a material impact on our financial statements, including financial statements for previous periods.

Our future success depends on our ability to enter into successful collaboration arrangements with third parties in order to develop new products and new indications for existing products that achieve regulatory approval for commercialization

For our business model to succeed, we must continually develop new products or achieve new indications for the use of our existing products. As a part of that process, we rely on third parties for clinical testing and certain other product development activities especially in the area of our glaucoma programs. In order to pursue our anti-inflammatory and glaucoma programs, ISV-205, we must enter into a third-party collaboration agreement for the development, marketing and sale thereof. There can be no assurance that we will be successful in finding a corporate partner for our ISV-205 programs or that any collaboration will be successful, either of which could significantly harm our business. If we are to develop and commercialize our product candidates successfully, including ISV-205, we will be required to enter into arrangements with one or more third parties that will:

- provide for Phase 2 and/or Phase 3 clinical testing;
- obtain or assist us in other activities associated with obtaining regulatory approvals for our product candidates; and
- market and sell our products, if they are approved.

In December 2003, we completed the sale of our drug candidate ISV-403 for the treatment of ocular infections to Bausch & Lomb Incorporated. Bausch & Lomb has assumed all future ISV-403 development and commercialization expenses and is responsible for all development activities, with our assistance, as appropriate. Our ability to generate royalties from this agreement will be dependent upon Bausch & Lomb's ability to complete the development of ISV-403, obtain regulatory approval for the product and successfully market it. In addition, under the Bausch & Lomb Purchase Agreement, we also have certain potential indemnification obligations to Bausch & Lomb in connection with the asset sale which, if triggered, could significantly harm our business and our financial position.

Our marketing and sales efforts related to our OcuGene glaucoma genetic test have been significantly curtailed. Any future activities would be pursued using external resources including:

- a network of key ophthalmic clinicians; and
- other resources with ophthalmic expertise.

We may not be able to enter into or maintain arrangements with third parties with ophthalmic or diagnostic industry experience on acceptable terms or at all. If we are not successful in concluding such arrangements on

acceptable terms, or at all, we may be required to establish our own sales force and expand our marketing organization significantly, despite the fact that we have no experience in sales, marketing or distribution. Even if we do enter into collaborative relationships these relationships can be terminated, thereby forcing us to seek alternatives. We may not be able to build a marketing staff or sales force and our sales and marketing efforts may not be cost-effective or successful.

While we expect to enter into additional partnering and collaborative arrangements in the future, such arrangements could include the exclusive licensing or sale of certain assets or the issuance of securities, which may adversely affect our future financial performance and the market price of our Common Stock. We cannot assure you that such arrangements will be beneficial to us. The success of our partnering and collaboration arrangements will depend upon many factors, including:

- the progress and results of the review of our NDAs by the FDA;
- the progress and results of our preclinical and clinical testing;
- our ability to establish additional corporate partnerships to develop, manufacture and market our potential products;
- the progress of our research and development programs;
- the outcome of possible future legal actions;
- the cost of maintaining or expanding a marketing organization for OcuGene and the related promotional activities;
- changes in, or termination of, our existing collaboration or licensing arrangements;
- whether we manufacture and market any of our other products ourselves;
- the time and cost involved in obtaining regulatory approvals;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- competing technological and market developments; and
- the purchase of additional capital equipment.

Physicians and patients may not accept and use our products

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

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

Because we expect sales of our current product candidates, if approved, to generate substantially all of our product revenues for the foreseeable future, the failure of any of these drugs, particularly AzaSite, to find market acceptance would harm our business and could require us to seek additional financing.

Questions concerning our financial condition may cause customers and current and potential partners to reduce or not conduct business with us

Our recent and on-going financial difficulties, and concerns regarding our ability to continue operations, even if we are able to raise additional funding, may cause current and potential customers and partners to decide not to conduct business with us, to reduce or terminate the business they currently conduct with us, or to conduct business

with us on terms that are less favorable than those customarily offered by them. In such event, our sales would likely decrease, our costs could increase, our product development and commercialization efforts would suffer and our business will be significantly harmed.

We may require additional licenses or be subject to expensive and uncertain patent litigation in order to sell AzaSite in the United States and/or Europe

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 not unusual in the pharmaceutical and biotech industry, from time to time we receive notices from third parties alleging various challenges to our patent rights, and we investigate the merits of each allegation that we receive. Such conflicts could invalidate our issued patents, limit the scope of the patents, if any, 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 issue patents that cover our activities to other companies, we may not be able to obtain licenses to these patents at all, or at a reasonable cost, or be able to develop or obtain alternative technology. If we do not obtain such licenses, we could encounter delays in or be precluded altogether from introducing products to the market.

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 emerging companies such as ours without significant existing revenue streams or other cash resources. We have also agreed to indemnify our licensees against infringement claims by third parties related to our technology, which could result in additional litigation costs and liability for us. In addition, our efforts to protect or defend our proprietary rights may not be successful or, even if successful, may result in substantial cost to us, thereby utilizing our limited resources for purposes other than product development and commercialization.

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

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

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

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

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

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

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

It is difficult to evaluate our business because we are in an early stage of development and our technology is untested

We are in an early stage of developing our business, particularly with respect to commercializing our products. We have only received an insignificant amount of royalties from the sale of one of our products, an over-the-counter dry eye treatment, and in 2002 we began to receive a small amount of revenues from the sale of our OcuGene glaucoma genetic test. With respect to our leading product candidate, AzaSite, the FDA must approve our NDA. Before regulatory authorities grant us marketing approval for additional products, we need to conduct significant additional research and development and preclinical and clinical testing. All of our products, including AzaSite, are subject to risks that are inherent to products based upon new technologies. These risks include the risks that our products:

- are found to be unsafe or ineffective;
- fail to receive necessary marketing clearance from regulatory authorities;
- even if safe and effective, are too difficult or expensive to manufacture or market;
- are unmarketable due to the proprietary rights of third parties; or
- are not able to compete with superior, equivalent, more cost-effective or more effectively promoted products offered by competitors.

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

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

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

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

We have incurred significant operating losses since our inception in 1986 and have pursued numerous drug development candidates that did not prove to have commercial potential. As of December 31, 2006, our accumulated deficit was approximately $153.1 million. We expect to incur net losses for theforeseeable future or until we are able to achieve significant royalties or other revenues from sales of our products. In addition, we recognize revenue when all services have been performed and collectibility is reasonably assured. Accordingly, revenue for sales of OcuGene

may be recognized in a later period than the associated recognition of costs of the services provided, especially during the initial launch of the product. In addition, due to this delay in revenue recognition, our revenues recognized in any given period may not be indicative of the then-current viability and market acceptance of our OcuGene product.

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 our leading product candidate AzaSite.

We may not successfully manage growth

Even if we are able to raise additional funding and gain FDA approval for additional products, including AzaSite, our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our management and on our administrative, operational and financial resources. To manage this growth, we will have to expand our facilities, augment our operational, financial and management systems and hire and train additional qualified personnel, all of which will cause us to incur significant additional expense. If we are unable to manage our growth effectively, our business would be harmed.

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

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

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

We have no experience in performing the analytical procedures related to genetic testing and have established an exclusive commercial agreement with a third party to perform these procedures for our OcuGene glaucoma genetic test; If we are unable to maintain this arrangement, and are unable to establish new arrangements with third parties, we will have to establish our own regulatory compliant analytical process for genetic testing and may not have the financial resources to do so

We have no experience in the analytical procedures related to genetic testing. We have entered into an agreement with Quest Diagnostics Incorporated, or Quest, under which Quest exclusively performs OcuGene

genetic analytical procedures at a commercial scale in the United States. Accordingly, we are reliant on Quest for all of our OcuGene analytical procedures. If we are unable to maintain this arrangement, we would have to contract with another clinical laboratory or would have to establish our own facilities. We cannot assure you that we will be able to contract with another laboratory to perform these services on a commercially reasonable basis, or at all.

Clinical laboratories must adhere to Clinical Laboratory Improvement Amendments, or CLIA, which are regulations that are strictly enforced by the FDA on an ongoing basis through the FDA's facilities inspection program. Should we be required to perform the analytical procedures for genetic testing ourselves, we:

- will be required to expend significant amounts of capital to install an analytical capability;
- will be subject to the regulatory requirements described above; and
- will require substantially more additional capital than we otherwise may require.

We cannot assure you we will be able to successfully enter into another genetic testing arrangement or perform these analytical procedures ourselves on a cost-efficient basis, or at all.

We rely on a sole source for some of the raw materials in our products, including AzaSite, and the raw materials we need may not be available to us

We currently have a single supplier for azithromycin, the active drug incorporated into our AzaSite product candidate. The supplier has a Drug Master File on the compound with the FDA and is subject to the FDA's review and oversight. If this supplier failed or refused to continue to supply us, if the FDA were to identify issues in the production of the drug that the supplier was unable to resolve quickly and cost-effectively, or if other issues were to arise that impact production, our ability to commence the commercial sale of AzaSite if and when it is approved, could be interrupted, which would significantly harm our business prospects. Additional suppliers for this drug exist, but qualification of an alternative source could be time consuming, expensive and could harm our business. There is also no guarantee that these additional suppliers can supply sufficient quantities at a reasonable price, or at all.

Under the Inspire License we will be the supplier of azithromycin to Inspire for the manufacture of AzaSite in the United States and Canada. If our supply becomes interrupted this will also interrupt the supply of the drug to Inspire until either of the companies are able to obtain a new supplier. While we are required to maintain a certain level of inventory of the raw material to support Inspire's manufacturing needs, this amount may not be sufficient to prevent an interruption in the availability of the product and would harm our ability to receive royalties. In the event of a disruption in the our supply of azithromycin to Inspire, Inspire is entitled to use a secondary source at our expense.

SSP is the sole source for the active drug incorporated into the ISV-403 product candidate we sold to Bausch & Lomb for further development and commercialization. SSP has submitted a Drug Master File on the compound with the FDA and is subject to the FDA's review and oversight. If SSP is unable to obtain and maintain FDA approval for their production of the drug or is otherwise unable or unwilling to supply Bausch & Lomb with sufficient quantities of the drug, Bausch & Lomb's ability to continue with the development, and potentially the commercial sale if the product is approved, of ISV-403 would be interrupted or impeded, and our future royalties from commercial sales of the ISV-403 product could be delayed or reduced and our business could be harmed.

In addition, certain of the raw materials we use in formulating our DuraSite drug delivery system are available only from Noveon Corporation, or Noveon. Although we do not have a current supply agreement with Noveon, to date we have not encountered any difficulties obtaining necessary materials from them. Any significant interruption in the supply of these raw materials could delay our clinical trials, product development or product sales, including sales of AzaSite, and could harm our business.

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

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

finished products may harm our clinical trials, regulatory filings, market introduction and subsequent sales of our products.

We have a contract with Cardinal Health, the manufacturer of our AzaSite Phase 3 clinical trial supplies and registration batches, to validate their production line for commercial scale batches and to manufacture the required validation batches for FDA review. Additionally, we have entered into a commercial manufacturing agreement with Cardinal Health for an initial four-year period. Under the Inspire License we will assist Inspire in establishing its own commercial manufacturing agreement with Cardinal Health for production of AzaSite upon approval of the AzaSite NDA. Other commercial manufacturers exist and we currently believe that we, or Inspire, could obtain alternative commercial manufacturing services if required. However, qualification of another manufacturer, transfer of the manufacturing process and regulatory approval of such a site would be costly and time consuming and would adversely impact Inspire's potential market introduction and subsequent sales of AzaSite, which would impact our potential royalty revenues. Cardinal Health's facility and the line that will be used to produce the AzaSite units may be subject to inspection by the FDA prior to the approval of the related NDA that we submitted to the FDA in June 2006. While we believe Cardinal Health will be prepared for the inspections, they could encounter delays or difficulties in preparing for, or during, the inspection which would adversely impact Inspire's potential market introduction and subsequent sales of AzaSite.

We currently contract with a third party to assemble the sample collection kits used in our OcuGene glaucoma genetic test. If our assembler should encounter significant delays or we have difficulty maintaining our existing relationship, or in establishing a new one, our sales of this product could be adversely affected.

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

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

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

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

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

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

The market for our product candidates is characterized by intense competition and rapid technological advances. If our product candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will be harmed.

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

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

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

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

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

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

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

Our research, development and manufacturing processes involve the controlled use of small amounts of hazardous solvents used in pharmaceutical development and manufacturing, including acetic acid, acetone, acrylic acid, calcium chloride, chloroform, dimethyl sulfoxide, ethyl alcohol, hydrogen chloride, nitric acid, phosphoric acid and other similar solvents. We retain a licensed outside contractor that specializes in the disposal of hazardous materials used in the biotechnology industry to properly dispose of these materials, but we cannot completely eliminate the risk of accidental contamination or injury from these materials. Our cost for the disposal services rendered by our outside contractor was approximately $11,800 and $7,400 for the years ended 2006 and 2005, respectively. In the event of an accident involving these materials, we could be held liable for any damages that result, and any such liability could exceed our resources. Moreover, as our business develops we may be required to incur significant costs to comply with federal, state and local environmental laws, regulations and policies, especially to the extent that we manufacture our own products.

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

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

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

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

As of December 31, 2006, our management and principal stockholders together beneficially owned approximately 25% of our outstanding shares of Common Stock. In addition, investors in our March/June 2004 and May 2005 private placements, as a group, owned approximately 22% of our outstanding shares of Common Stock as of December 31, 2006. If such investors were to exercise the warrants they currently hold, assuming no additional acquisitions, sales or distributions, such investors would own approximately 32% of our outstanding shares of Common Stock based on their ownership percentages as of December 31, 2006. As a result, these two groups of stockholders, acting together or as individual groups, may be able to exert significant control on matters requiring approval by our stockholders, including the election of all or at least a majority of our Board of Directors, amendments to our charter, and the approval of business combinations and certain financing transactions.

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

The market prices for securities of biopharmaceutical and biotechnology companies, including ours, have been highly volatile. The market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. In addition, future announcements and circumstances, such as our current financial condition, the audit report included in our annual report on Form 10-K for the year ended December 31, 2006 that included an explanatory paragraph referring to our recurring operating losses and a substantial doubt about our ability to continue as a going concern, our ability to obtain new financing, the status of our relationships or proposed relationships with third-party collaborators, the terms of any financing we are able to raise, the results of testing and clinical trials, developments in patent or other proprietary rights of us or our competitors, 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.

Future equity financings that we may pursue as well as the exercise of outstanding options and warrants could result in dilution to our current holders of Common Stock and cause a significant decline in the market price for our Common Stock. In connection with our December 2005 and January 2006 Private Placement of Notes and Warrants, we issued Warrants to purchase 1,460,000 shares of our Common Stock. In connection with our August 2006 Private Placement we issued warrants to purchase 958,015 shares of our Common Stock.

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.

In addition, terrorist attacks in the United States and abroad, United States retaliation for these attacks, the war in Iraq or potential worldwide economic weakness and the related decline in consumer confidence have had, and may continue to have, an adverse impact on the United States and world economy. These and similar events, as well as fluctuations in our operating results and market conditions for biopharmaceutical and biotechnology stocks in general, could have a significant effect on the volatility of the market price for our Common Stock, the future price of our Common Stock and on our ability to raise additional financing.

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

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

Legislative actions, higher insurance costs and potential new accounting pronouncements are likely to impact our future financial position and results of operations

There have been regulatory changes, including the adoption of the Sarbanes-Oxley Act of 2002, and there may be potential new accounting pronouncements or regulatory rulings, which will have an impact on our future financial position and results of operations. Beginning with our 2006 fiscal year we must comply with Section 404 of the Sarbanes-Oxley Act of 2002 regarding certification of our internal control over financial reporting, which has and will continue to significantly increase our compliance costs. The Sarbanes-Oxley Act of 2002 and other rule changes and proposed legislative initiatives are likely to continue to increase general and administrative costs. In addition, insurance costs, including health, workers' compensation and directors and officers' insurance costs, have

been dramatically increasing and insurers are likely to increase rates as a result of high claims rates over the past year and our rates are likely to increase further in the future. These and other potential changes could materially increase the expenses we report under generally accepted accounting principles, and adversely affect our operating results.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

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

Item 3. Legal Proceedings

None

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

On October 3, 2006, we held our Annual Meeting of Stockholders at which our stockholders approved:

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

	For Election	Withheld
S. Kumar Chandrasekaran, Ph.D.	61,511,935	1,046,154
Mitchell H. Friedlaender, M.D.	61,175,347	1,382,742
John L. Mattana	61,209,935	1,348,154
Jon S. Saxe	61,163,397	1,394,692
Anders P. Wiklund	61,170,467	1,387,622

(2) An amendment to our Restated Certificate of Incorporation to increase the number of shares of our common stock authorized for issuance by an additional 120,000,000 shares, resulting in an aggregate of 240,000,000 shares of authorized common stock. Such proposal received 53,177,374 votes for approval, 9,355,037 votes against approval, and 25,677 votes abstaining.

(3) The ratification of our audit committee's appointment of Burr, Pilger & Mayer LLP as our independent public accountants for the fiscal year ending December 31, 2006. Such proposal received 62,310,482 votes for ratification, 111,204 votes against ratification and 136,400 abstentions.

Executive Officers of the Company

As of March 15, 2007, our executive officers and other senior management were as follows:

Name	Age	Title
S. Kumar Chandrasekaran, Ph.D.	64	Chairman of the Board, President, Chief Executive Officer and Chief Financial Officer
Lyle M. Bowman, Ph.D.	58	Vice President, Development and Operations
Ronald H. Carlson	53	Vice President, Regulatory and Quality
David F. Heniges	63	Vice President and General Manager, Commercial Opportunities
Sandra C. Heine	45	Vice President, Finance and Administration
Erwin C. Si, Ph.D.	53	Senior Director, Preclinical Research

S. Kumar Chandrasekaran joined us in September 1987 as Vice President, Development. From 1988 to 1989, Dr. Chandrasekaran served as Vice President, Research and Development. From 1989 to 1993, he served as President and Chief Operating Officer. Since August 1993, Dr. Chandrasekaran has served as Chairman of the Board of Directors, President, Chief Executive Officer and, since January 1999, as Chief Financial Officer, a position he also held from December 1995 to December 1997. Dr. Chandrasekaran holds a Ph.D. in Chemical Engineering from the University of California, Berkeley.

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

Ronald Carlson joined us in April 2006 as Vice President, Regulatory and Quality. From 1999 to 2006, Dr. Carlson worked at XOMA LLC, a biotechnology company focused on the development of therapeutic antibodies, where he held positions of Vice President of Quality and Senior Director of Regulatory Affairs. Dr. Carlson was also Vice President of Development at Berkeley HeartLab Inc. and has held managerial positions at Bayer, Isis, Berlex, and Genentech. Dr. Carlson holds a Bachelor of Science in both Chemistry and Mathematics and a Ph.D. in Chemistry from Southern Illinois University.

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

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

Erwin C. Si joined us in April 1989 as Manager of Pharmacology and Toxicology. From 1992 to 1996, he served as Manager of Drug Discovery. From 1996 to 1999, he served as Principal Scientist. Since October 1999, he has served as Senior Director of Preclinical Research. Dr. Si holds a Ph.D. in Pharmacology and Toxicology from Purdue University.

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

PART II

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

Market Information

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

2006	High	Low
First Quarter	$2.17	$0.90
Second Quarter	$2.69	$1.53
Third Quarter	$1.90	$1.26
Fourth Quarter	$1.88	$1.27

2005	High	Low
First Quarter	$0.92	$0.48
Second Quarter	$0.87	$0.42
Third Quarter	$0.70	$0.49
Fourth Quarter	$0.95	$0.61

Holders

As of March 13, 2007, we had approximately 250 stockholders of record of our Common Stock. On March 13, 2007, the last sale price reported on The American Stock Exchange for our common stock was $1.45 per share.

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.

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 consolidated financial statements and notes thereto and the Management's Discussion and Analysis of Financial Condition and Results of Operations contained elsewhere in this Annual Report on Form 10-K. The following table sets forth selected consolidated financial data for us for the five years ended December 31, 2006 (in thousands except per share amounts):

	Year Ended December 31,				
	2006	2005	2004	2003	2002
Consolidated Statements of Operations Data					
Revenues	$ 2	$ 4	$ 542	$ 134	$ 36
Cost of goods	28	14	14	20	114
Operating expenses:					
Research and development, net	8,890	10,690	6,788	4,007	5,991
Selling, general and administrative	6,182	4,510	3,826	3,450	4,942
Total expenses	15,072	15,200	10,614	7,457	10,933
Gain on sale of assets	—	—	4,616	1,153	—
Interest (expense) and other income, net	(1,513)	(5)	(44)	(561)	62
Net income loss	(16,611)	(15,215)	(5,514)	(6,751)	(10,949)
Non cash preferred dividend	—	—	—	221	48
Net income loss applicable to common stockholders	$ (16,611)	$ (15,215)	$ (5,514)	$ (6,972)	$ (10,997)
Basic and diluted loss per share applicable to common stockholders	$ (0.19)	$ (0.21)	$ (0.11)	$ (0.27)	$ (0.44)
Shares used to calculate basic and diluted net loss per share	88,339	72,647	47,984	25,767	24,997

	December 31,				
	2006	2005	2004	2003	2002
Consolidated Balance Sheet Data					
Cash and cash equivalents, unrestricted	$ 987	$ 4,027	$ 5,351	$ 1,045	$ 1,179
Working capital	(6,836)	(3,424)	3,515	(6,434)	353
Total assets	2,439	5,079	5,696	1,405	1,866
Long term notes payable	—	—	—	16	10
Convertible preferred stock	—	—	—	—	2,048
Accumulated deficit	(153,062)	(136,451)	(121,236)	(115,722)	(108,750)
Total stockholders' equity (deficit)	(6,302)	(2,545)	3,601	(6,200)	887

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 Operation

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

Overview

We are an ophthalmic product development company focused on ophthalmic pharmaceutical products based on our proprietary DuraSite® eyedrop-based drug delivery technology, as well as the development of genetically-based technologies for the diagnosis, prognosis and management of glaucoma.

We face significant challenges related to our lack of financial resources. We only expect our current cash to enable us to continue our operations as currently planned until approximately the end of June 2007. Our independent auditors included an explanatory paragraph in their audit report related to our consolidated financial statements for the fiscal year ended December 31, 2006 referring to our recurring operating losses and a substantial doubt about our ability to continue as a going concern.

With our existing resources we are focusing our research and development and commercial efforts on the following:

- AzaSite™ (ISV-401), a DuraSite formulation of azithromycin, to serve as a broad spectrum ocular antibiotic; and

- AzaSite Plus™ (ISV-502), a DuraSite formulation of azithromycin and a steroid for inflammation and pain.

In June 2006, we completed the compilation and assembly of an AzaSite NDA, and submitted the documentation to the FDA. Based on the FDA's Prescription Drug User Fee Act, or PDUFA, we anticipate a ruling by the FDA on the potential approval of AzaSite by the end of April 2007.

From our inception through the end of 2001, we did not receive any revenues from the sale of our products, other than a small amount of royalties from the sale of our AquaSite product by CIBA Vision and Global Damon. In the fourth quarter of 2001, we commercially launched our OcuGene glaucoma genetic test and early in 2002 we began to receive a small amount of revenues from the sale of this test. With the exception of 1999 and the six month period ended June 30, 2004, we have been unprofitable since our inception due to continuing research and development efforts, including preclinical studies, clinical trials and manufacturing of our product candidates. We have financed our research and development activities and operations primarily through private and public placements of equity and debt securities, issuance of convertible debentures, collaborative agreements and bridge loans.

Recent Developments

On February 15, 2007, we entered into a worldwide, exclusive, royalty-bearing licensing agreement with Pfizer, under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus. Under the Pfizer License, we are required to pay Pfizer a single digit royalty based on net sales of the licensed products and to use reasonable commercial efforts to seek regulatory approval for and market licensed products. We can grant sublicenses under the Pfizer License, subject to Pfizer's prior approval, which the Pfizer License provides shall not be unreasonably withheld.

On February 15, 2007, we entered into a license agreement with Inspire, under which we licensed to Inspire exclusive development and commercialization rights, under our AzaSite™ patent rights and certain know-how, for topical anti-infective products containing azithromycin as the sole active ingredient for human ocular or ophthalmic indications in the Territory. The Inspire License also provides for nonexclusive licenses under our DuraSite® patent rights, container patent rights, Columbia patent rights and certain know-how in the same field of use as described above as well as an exclusive sublicense under the Pfizer patent rights that we have licensed under the Pfizer License discussed above.

Upon the closing of the Inspire License, Inspire paid us an upfront license fee of $13 million and is obligated to pay us an additional $19 million upon regulatory approval and the approval of an acceptable label for any Subject Product by the FDA. The royalty rate will be 20% of net sales in the first two years of commercialization and 25% thereafter. For five years after the first year of commercial sale, Inspire is required to pay us the greater of the running royalty discussed above or certain tiered minimum royalties. The royalties from Inspire are subject to certain reductions, but will in no event fall below a low single digit royalty based on applicable net sales.

We also entered into a trademark license agreement with Inspire on February 15, 2007 under which we granted to Inspire an exclusive license to the AzaSite™ trademark and domain name and a nonexclusive license to the DuraSite® trademark in connection with the commercialization of AzaSite and other subject products in the Territory under the terms of the Inspire License.

We also entered into a supply agreement with Inspire on February 15, 2007 for the active pharmaceutical ingredient azithromycin. We had previously entered into a third party supply agreement for the production of such active ingredient. Under the Supply Agreement, we agreed to supply Inspire's requirements of such active ingredient, pursuant to certain forecasting and ordering procedures.

On December 22, 2006, the holders of our Senior Notes extended the maturity date under such Senior Notes from December 30, 2006 to February 15, 2007. On February 15, 2007, we redeemed and repaid in full the $7,325,739 in principal and interest due under our Senior Notes. Such funds were paid from a portion of the upfront license fee we received under the Inspire License. In connection with the redemption and cancellation of our Senior Notes, all liens on our assets, including our intellectual property, were automatically released and all of our obligations to the holders of the Senior Notes under the Amended and Restated Security Agreement, dated as of December 30, 2005 and the Intercreditor and Collateral Agency Agreement, dated as of December 30, 2005 were terminated. Of such Senior Notes redeemed, $231,000 in aggregate principal amount was held by our Chief Executive Officer. We also redeemed and cancelled that certain amended and restated promissory note dated as of

December 30, 2005, with an aggregate principal amount of $35,000 issued to our Vice President, Finance and Administration.

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

Reclassifications

In 2006, we changed our classification of patent costs to be a selling, general and administrative expense, which had previously been classified as a research and development expense. This is consistent with Statement of Financial Accounting Standard ("SFAS") No. 2 on Research and Development costs. SFAS No. 2 requires that research and development costs exclude legal work in connection with patent applications, litigation and the sale or licensing of patents. We made the change to better reflect the expenses incurred related to active research and development activities as legal expenses which are more administrative in nature and accordingly should be charged to selling, general and administrative expense. The impact of this change on our previously reported research and development and selling, general and administrative expenses in the years ended December 31, 2005 and 2004 is as follows:

	Year Ended December 31, 2005	Year Ended December 31, 2004
	(in thousands)	
Research and development as previously reported	$ 11,321	$ 7,273
Reclassification of patent expense	(631)	(485)
Research and development	$ 10,690	$ 6,788
Selling, general and administrative as previously reported	$ 3,879	$ 3,341
Reclassification of patent expense	631	485
Selling, general and administrative	$ 4,510	$ 3,826

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 up-front fees from licensing and similar arrangements over the expected term of the related research and development services using the straight-line method. When changes in the expected term of ongoing services are identified, the amortization period for the remaining fees is appropriately modified.

Revenue related to performance milestones is recognized when the milestone is achieved based on the terms set forth in the related agreements.

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

During the year ended 2004, we recognized cost reimbursements as contract and other revenue in accordance with EITF 01-14, "Income Statement Characterization of Reimbursement for Out of Pocket Expenses Incurred." We recognize the received cost sharing payments when persuasive evidence of an arrangement exists, the services have been rendered, the fee is fixed or determinable and collectibility is reasonably assured.

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

Revenue related to sales of our product, the OcuGene glaucoma genetic test, is recognized when all related services have been rendered and collectibility is reasonably assured. Accordingly, revenue for sales of OcuGene may be recognized in a later period than the associated recognition of costs of the services provided, especially during the initial launch of the product. The revenue in connection with the sale of ISV-403 to B&L was recognized over the contract period.

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

Cost of revenue. We recognize the cost of inventory shipped and other costs related to our OcuGene glaucoma genetic test when they are incurred.

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

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

Inventory. Our inventories are stated at the lower of cost or market. The cost of the inventory is based on the first-in first-out method. If the cost of the inventory exceeds the expected market value a provision is recorded for the difference between cost and market. At December 31, 2005, our inventory solely consisted of OcuGene kits which are considered finished goods.

Results of Operations

Revenues.

We had total net revenues of $2,000, $4,000, and $542,000 for the years ended December 31, 2006, 2005 and 2004, respectively, from contract research activities and sales of OcuGene. Our revenue in 2004 was due to contract research activities conducted for Bausch & Lomb in 2004 under the ISV-403 Asset Purchase Agreement. We are no longer providing services to Bausch & Lomb and we do not expect to derive revenue from these activities in 2007 or future years.

Cost of goods.

Our cost of goods of $28,000, $14,000 and $14,000 for 2006, 2005 and 2004, respectively, reflect the cost of OcuGene tests performed as well as the cost of sample collection kits distributed for use.

Research and development, net.

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

Research and development expenses increased to $10.7 million in 2005 from $6.8 million in 2004. The majority of this increase represents increases in the cost of the clinical research organizations and microbiological testing

related to our AzaSite Phase 3 clinical trials. The remainder of the increase mainly reflects costs related to consultants and temporary labor to assist with the preparation of the AzaSite NDA.

Our R&D activities can be separated into two major segments, research and clinical development. Research includes activities involved in evaluating a potential product, related pre-clinical 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 2006, 2005 and 2004 (in thousands):

	2006	2005	2004
Research	$3,291	$ 2,142	$2,390
Clinical development	5,599	8,548	4,398
Total research and development	$8,890	$10,690	$6,788

Although the majority of our personnel were focused on our AzaSite program in 2006, due to our limited personnel and the number of projects that we are developing including our AzaSite Plus program, our personnel are involved in a number of projects at the same time. Accordingly, the majority of our R&D expenses are not linked to a specific project but are allocated across projects, based on personnel time expended on each project. Accordingly, the allocated costs may not reflect the actual costs of each project.

The increase in research activities in 2006 compared to 2005 mainly reflected activities to support the filing of the AzaSite NDA, preparation for commercial manufacture of AzaSite, preclinical testing to support the AzaSite Plus IND, manufacture of AzaSite Plus Phase 1 clinical units and preparation for manufacture of Phase 3 AzaSite Plus clinical units at our contract manufacturing site. The decrease in research activities in 2005 compared to 2004 mainly reflected the decrease in manufacturing activities as expenses related to the production of clinical supplies for the Phase 3 AzaSite trials were incurred mainly in 2004.

The decrease in clinical development expenses in 2006 as compared to 2005 reflects the completion of the AzaSite Phase 3 clinical trials early in the year. This reduction was partially offset by the increase in headcount, consultants and outside services, primarily in the regulatory departments, to support the preparation and filing of our AzaSite NDA. Additionally, in 2006 we filed our AzaSite Plus IND and conducted a Phase 1 clinical trial. The cost of such a trial is significantly less than a Phase 3 trial mainly due to the few number of patients included in a Phase 1 trial. The majority of the increase from 2004 to 2005 is related to our AzaSite Phase 3 clinical trials which were initiated in 2004.

Other than AzaSite, most of our projects are in the early stages of the product development cycle and may not result in commercial products. Projects in development may not proceed into clinical trials due to a number of reasons even though the project looks promising early in the process. Once a project reaches clinical trials it may be found to be ineffective or there may be harmful side effects. Additionally, during the development cycle, other companies may develop new treatments that decrease the market potential for our project or be issued patents that require us to negotiate a license or cease pursuing one of our products and we may decide not to proceed. Other factors including the cost of manufacturing at a commercial scale and the availability of quality manufacturing capabilities could negatively impact our ability to bring the project to the market. Also, our business strategy is to license projects to third parties to complete the development cycle and to market and sell the product. If we are unable to enter into collaborative arrangements for any product candidate, our ability to commercialize the product may be slowed or we may decide not to proceed with that candidate. These collaborative arrangements may either speed the development or they may extend the anticipated time to market. Because of these factors, as well as others, we cannot be certain if, or when, our projects in development will complete the development cycle and be commercialized.

Selling, general and administrative.

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

Selling, general and administrative expenses increased to $4.5 million in 2005 from $3.8 million in 2004. Legal expenses increased in 2005 mainly due to costs associated with the Bristol arbitration which was settled in 2005. Additionally, in 2005 costs were incurred for marketing studies related to the AzaSite and AzaSite Plus product candidates.

Interest (expense) and other income, net.

Interest (expense) and other income, net was an expense of $1.5 million, $5,000 and $44,000 in 2006, 2005 and 2004, respectively. The increased expense in 2006 mainly reflects accrued interest payable on our short-term Senior Secured Notes issued in December 2005 and January 2006 and the accretion of the value of the debt discount related to the warrants issued as part of the note financing. The decrease in 2005 from 2004 mainly reflects the lower average balance of debt outstanding during 2005 compared to 2004 as we did not close the December tranche of the Senior Secured Notes until December 30, 2005. Any interest earned or paid in the future will be dependent on our ability to raise additional funding or execute collaborative or other partnering agreements and prevailing interest rates.

Liquidity and Capital Resources

We have financed our operations since inception primarily through private placements and public offerings of debt and equity securities, equipment and leasehold improvement financing, other debt financing and payments from corporate collaborations. At December 31, 2006, our unrestricted cash and cash equivalents were $1.0 million. It is our policy to invest our cash and cash equivalents in highly liquid securities, such as interest-bearing money market funds, Treasury and federal agency notes and corporate debt.

Our auditors have included an explanatory paragraph in their audit report referring to our recurring operating losses and a substantial doubt about our ability to continue as a going concern. Absent additional funding from private or public equity or debt financings, collaborative or other partnering arrangements, including under the Inspire License, asset sales, or other sources, we expect that our cash on hand, including cash received from the Inspire License in February 2007, a refund of approximately $767,000 from the FDA related to our AzaSite NDA filing, anticipated cash flow from operations and current cash commitments to us will only be adequate to fund our operations until approximately the end of June 2007. If we are unable to secure sufficient additional funding prior to that time, we will need to cease operations and liquidate our assets. Our financial statements were prepared on the assumption that we will continue as a going concern and do not include any adjustments that might result should we be unable to continue as a going concern.

Even if we are able to obtain additional financing in order to continue long-term operations beyond approximately the end of June 2007, we will require and will seek additional funding through collaborative or other partnering arrangements, public or private equity or debt financings and from other sources. However, there can be no assurance that we will obtain interim or longer-term financing or that such funding, if obtained, will be sufficient to continue our operations as currently conducted or in a manner necessary for the continued development of our products or the long-term success of our company. If we raise funds through the issuance of debt securities, such debt will likely be secured by a security interest or pledge of all of our assets, will require us to make principal and interest payments, would likely include the issuance of warrants and may subject us to restrictive covenants. If we raise funds through one or more equity offerings, our stockholders may suffer substantial dilution.

For the years ended December 31, 2006, 2005 and 2004, cash used for operating activities was $16.2 million, $13.4 million and $10.0 million, respectively. Cash used in investing activities was $322,000, $137,000 and $183,000 primarily related to cash outlays for additions to laboratory and other equipment and a change in restricted cash during 2005 and 2004, respectively.

Cash provided by financing activities was $13.5 million, $12.2 million and $14.5 million for the years ending December 31, 2006, 2005 and 2004, respectively. In 2006 we received net proceeds of $5.8 million from the exercise of warrants, options and stock purchases under our employee stock purchase plan compared to $536,000 and $14,000 in 2005 and 2004, respectively.

The tables below set forth the amount of cash that we raised for fiscal years 2004 through 2006 from warrant and option exercises, stock purchases under our employee stock purchase plan, equity financings and debt financings.

Cash Received from Warrant and Option Exercises and Employee Stock Purchase Plan

Year	Net Proceeds
2006	$5.8 million
2005	$536,000
2004	$14,000

Cash Received from Private Placements of Equity Securities

Date	Net Proceeds	Shares of Common Stock Issued
August 2006	$5.8 million	4.8 million plus warrants to purchase 1.0 million shares
May 2005	$8.1 million	16.4 million plus warrants to purchase 4.9 million shares
March 2004	$15.1 million	33.0 million plus warrants to purchase 16.5 million shares

Cash Received from Private Placement of Notes

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

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

In addition to the above, 2005 and 2004 we repaid $73,000 and $621,000, respectively, of short-term notes payable to directors, members of senior management and other stockholders, which bear interest at rates from 2% to 12% and are due March 31, 2007. We received payments on a note to a stockholder of $168,000, $19,000, and $21,000 in 2006, 2005 and 2004, respectively. We also made $10,000 and $13,000 of payments on capital leases for certain laboratory equipment in 2006 and 2004, respectively.

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

We anticipate no material capital expenditures to be incurred for environmental compliance in fiscal year 2007. Based on our environmental compliance record to date, and our belief that we are current in compliance with applicable environmental laws and regulations, environmental compliance is not expected to have a material adverse effect on our operations.

Off-Balance Sheet Arrangements

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

Contractual Obligations

The following table summarizes our significant contractual obligations as of December 31, 2006 and the effect such obligations are expected to have on our liquidity and cash flows in the future periods. Some of these amounts

are based on management's estimate and assumptions about these obligations including their duration, the possibility of renewal and other factors. Because these estimates are necessarily subjective, our actual payments in the future may vary from those listed in this table.

	Payments Due by Period (in thousands)				
	Total	Less than 1 Year	1 – 3 Years	3 – 5 Years	More than 5 Years
Capital Lease Obligations(1)	$ 75	$ 18	$ 35	$ 22	$ —
Facilities Lease Obligations(2)	4,285	559	1,170	1,240	1,316
Purchase obligations(3)	676	676	—	—	—
Licensing agreement obligations(4)	220	20	40	40	120
Notes Payable(5)	6,566	6,566			
Accrued Interest(6)	702	702	—	—	—
Total commitments	$ 12,524	$ 8,541	$ 1,245	$ 1,302	$ 1,436

(1) We lease our telephones and telephone equipment under two capital lease agreements, which expire in 2011.

(2) We lease our facilities under a non-cancelable operating lease that expires in 2013.

(3) Purchase obligations include commitments related to clinical development, consulting contracts, equipment maintenance, and other significant purchase commitments.

(4) We have entered into certain license agreements that require us to make minimum royalty payments for the life of the licensed patents. The life of the patents that may be issued and covered by the license agreements cannot be determined at this time, but the minimum royalties due under such agreements are as noted for 2006 through 2017 and are approximately $20,000 per year.

(5) We repaid these notes in full in February 2007. See further discussion of our debt issuances above in "Liquidity."

(6) We have accrued interest related to our Notes Payable. This interest was paid in February 2007 when the related Notes were repaid in full.

Recent Accounting Pronouncements

In February 2006, the FASB issued Statement of Financial Accounting Standards No. 155, *Accounting for Certain Hybrid Financial Instruments — an amendment of FASB Statements No. 133 and 140* (SFAS No. 155). SFAS No. 155 permits an entity to measure at fair value any financial instrument that contains an embedded derivative that otherwise would require bifurcation. This statement is effective for all financial instruments acquired, issued, or subject to a remeasurement event occurring after the beginning of an entity's first fiscal year that begins after September 15, 2006, which is our fiscal year 2007. We do not expect the adoption of SFAS No. 155 to have a material impact on our consolidated financial statements.

In June 2006, the FASB issued FASB Interpretation No. (FIN) 48, *Accounting for Uncertainty in Income Taxes — An Interpretation of FASB Statement No. 109* (FIN48), which prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 will be effective for fiscal years beginning after December 15, 2006, which is our fiscal year 2007. We are currently in the process of evaluating the potential impact of adopting FIN 48 on our consolidated financial statements.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 157, *Fair Value Measurements* (SFAS No. 157), which defines fair value, establishes a framework for measuring fair value under GAAP, and expands disclosures about fair value measurements. SFAS No. 157 will be effective for fiscal years beginning after November 15, 2007, which is our fiscal year 2008. We have not yet evaluated the potential impact of adopting SFAS No. 157 on our consolidated financial statements.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 158, *Employers' Accounting for Pensions and Other Postretirement Benefits* (SFAS No. 158). SFAS No. 158 requires employers to recognize on their balance sheet an asset or liability equal to the over- or under-funded benefit obligation of each defined benefit pension and other postretirement plan and to recognize as a component of other comprehensive income, net of tax, the gains or losses and prior service costs or credits that arise during the period but are not

recognized as components of net periodic benefit cost. Amounts recognized in accumulated other comprehensive income, including the gains or losses, prior service costs or credits, and the transition asset or obligation remaining from the initial application of (i) FASB Statement No. 87, *Employers' Accounting for Pensions* and (ii) FASB Statement No. 106, *Employers' Accounting for Postretirement Benefits Other Than Pensions,* are adjusted as they are subsequently recognized as components of net periodic benefit cost pursuant to the recognition and amortization provisions of those statements. This change in balance sheet reporting is effective for fiscal years ending after December 15, 2006 for public companies, which is our fiscal year 2006. SFAS No. 158 also eliminates the ability to use an early measurement date, commencing with fiscal years ending after December 15, 2008, which is our fiscal year 2008. The adoption of SFAS No. 158 did not have a material impact on our December 31, 2006 consolidated financial statements.

In September 2006, the SEC issued Staff Accounting Bulletin No. 108 ("SAB 108"), "Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements." SAB 108 is effective for fiscal years ending on or after November 15, 2006 and addresses how financial statement errors should be considered from a materiality perspective and corrected. The literature provides interpretive guidance on how the effects of the carryover or reversal of prior year misstatements should be considered in quantifying a current year misstatement. Historically there have been two common approaches used to quantify such errors: (i) the "rollover" approach, which quantifies the error as the amount by which the current year income statement is misstated, and (ii) the "iron curtain" approach, which quantifies the error as the cumulative amount by which the current year balance sheet is misstated. The SEC Staff believes that companies should quantify errors using both approaches and evaluate whether either of these approaches results in quantifying a misstatement that, when all relevant quantitative and qualitative factors are considered, is material. We adopted the provisions of SAB 108 in our 2006 fourth fiscal quarter and it had no impact on our consolidated financial statements.

In February 2007, the FASB issued FASB Statement No. 159, "The Fair Value Option for Financial Assets and Financial Liabilities—Including an amendment of FASB Statement No. 115" ("SFAS 159"). SFAS 159 creates a "fair value option" under which an entity may elect to record certain financial assets or liabilities at fair value upon their initial recognition. Subsequent changes in fair value would be recognized in earnings as those changes occur. The election of the fair value option would be made on a contract-by contract basis and would need to be supported by concurrent documentation or a preexisting documented policy. SFAS 159 requires an entity to separately disclose the fair value of these items on the balance sheet or in the footnotes to the financial statements and to provide information that would allow the financial statement user to understand the impact on earnings from changes in the fair value. SFAS 159 is effective for us beginning with fiscal year 2008. We are currently evaluating the impact that the adoption of SFAS 159 will have on our consolidated financial statements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

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

We invest our excess cash in investment grade, interest-bearing securities. At December 31, 2006, we had $1.0 million invested in interest bearing operating accounts. While a hypothetical decrease in market interest rates by 10 percent from the December 31, 2006 levels would cause a decrease in interest income, it would not result in a loss of the principal. Additionally, the decrease in interest income would not be material.

Item 8. Financial Statements and Supplementary Data

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

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
InSite Vision Incorporated

We have audited the accompanying consolidated balance sheets of InSite Vision Incorporated and its subsidiaries (the "Company") as of December 31, 2006 and 2005, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2006. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of InSite Vision Incorporated and its subsidiary as of December 31, 2006 and 2005, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2006, in conformity with accounting principles generally accepted in the United States of America.

As discussed in Note 1 to the consolidated financial statements, the Company's recurring losses from operations raise substantial doubt about its ability to continue as a going concern. Management's plans as to these matters are also described in Note 1. The 2006 consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

As discussed in Note 1 and Note 10 to the consolidated financial statements, on January 1, 2006 the Company changed its method of accounting for stock-based compensation as a result of adopting Statement of Financial Accounting Standards No. 123 (revised 2004), "Share-Based Payment" applying the modified prospective method.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of the Company's internal control over financial reporting as of December 31, 2006, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 15, 2007 expressed an unqualified opinion on management's assessment of, and the effective operation of, internal control over financial reporting.

/s/ BURR, PILGER, & MAYER LLP

Palo Alto, California
March 15, 2007

INSITE VISION INCORPORATED

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2006	2005
	(in thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 986	$ 4,027
Restricted cash and cash equivalents	75	75
Inventory	—	17
Deferred debt issuance cost	22	614
Prepaid expenses and other current assets	795	81
Total current assets	1,878	4,814
Property and equipment, at cost:		
Laboratory and other equipment	580	313
Leasehold improvements	5	73
Furniture and fixtures	77	10
	662	396
Accumulated depreciation	101	131
	561	265
Total assets	$ 2,439	$ 5,079
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Short-term notes payable to related parties, unsecured	$ 35	$ 35
Short-term notes payable to related parties, secured	231	231
Short-term notes payable, secured, (net of debt discount of $0 at December 31, 2006 and $491 at December 31, 2005)	6,300	3,809
Current portion of capital lease obligation	12	—
Accrued interest	702	3
Accounts payable	377	1,941
Accrued liabilities	381	1,167
Accrued compensation and related expense	648	388
Deferred rent	6	50
Total current liabilities	8,692	7,624
Capital lease obligation, less current portion	49	—
Total liabilities	8,741	7,624
Stockholders deficit		
Preferred stock, $0.01 par value, 5,000,000 shares authorized, none issued and outstanding at December 31, 2006 and 2005	—	—
Common stock, $0.01 par value, 240,000,000 and 120,000,000 shares authorized at December 31, 2006 and 2005, respectively; 93,284,934 issued and outstanding at December 31, 2006; 79,614,806 issued and outstanding at December 31, 2005	933	796
Additional paid-in capital	145,827	133,278
Notes receivable from stockholder	—	(168)
Accumulated deficit	(153,062)	(136,451)
Common stockholders' deficit	(6,302)	(2,545)
Total liabilities and stockholders' deficit	$ 2,439	$ 5,079

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2006	2005	2004
	(in thousands, except per share amounts)		
Revenues	$ 2	$ 4	$ 542
Cost of revenue	28	14	14
Gross margin	(26)	(10)	528
Operating expenses:			
Research and development(a)	8,890	10,690	6,788
Selling, general and administrative(a)	6,182	4,510	3,826
Total	15,072	15,200	10,614
Loss from operations	(15,098)	(15,210)	(10,086)
Gain on sale of assets	—	—	4,616
Interest (expense) and other income, net	(1,513)	(5)	(44)
Net loss	$ (16,611)	$ (15,215)	$ (5,514)
Net loss per share – basic and diluted	$ (0.19)	$ (0.21)	$ (0.11)
Shares used to calculate basic and diluted net loss per share	88,339	72,647	47,984
(a) Includes the following amounts related to stock based compensation:			
Research and development	$ 245	$ —	$ —
Selling, general and administrative	$ 565	$ —	$ —
	$ 810	$ —	$ —

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

	Preferred Stock	Common Stock	Additional Paid In Capital	Note Receivable From Stockholder	Accumulated Deficit	Total Stockholders' Equity (deficit)
			(dollars in thousands)			
Balances, December 31, 2003	**$ —**	**$ 293**	**$ 109,437**	**$ (208)**	**$ (115,722)**	**$ (6,200)**
Issuance of 19,623 shares of common stock from exercise of options and employee stock purchase plan	—	—	12	—	—	12
Issuance of 33,000,000 shares of common stock from private placement	—	330	14,781	—	—	15,111
Non-employee stock compensation	—	—	96	—	—	96
Issuance of 2,940 shares of common stock from exercise of warrants	—	—	2	—	—	2
Loan payment from stockholder	—	—	—	21	—	21
Issuance of 105,951 shares of common stock from conversion of notes payable	—	1	72	—	—	73
Net loss	—	—	—	—	(5,514)	(5,514)
Balances, December 31, 2004	**—**	**624**	**124,400**	**(187)**	**(121,236)**	**3,601**
Issuance costs related to 2004 private placement	—	—	(262)	—	—	(262)
Issuance of 65,647 shares of common stock from exercise of options and employee stock purchase plan	—	—	33	—	—	33
Issuance of 803,725 shares of common stock from exercise of warrants	—	8	495	—	—	503
Issuance of 16,363,626 shares of common stock from private placement	—	164	7,978	—	—	8,142
Non-employee stock compensation	—	—	14	—	—	14
Loan payment from stockholder	—	—	—	19	—	19
Issuance of warrants in connection with private placement of notes payable	—	—	620	—	—	620
Net loss	—	—	—	—	(15,215)	(15,215)
Balances, December 31, 2005	**—**	**796**	**133,278**	**(168)**	**(136,451)**	**(2,545)**
Issuance of 203,920 shares of common stock from exercise of options and employee stock purchase plan	—	2	131	—	—	133
Issuance of 8,676,132 shares of common stock from exercise of warrants, net	—	87	5,539	—	—	5,626
Issuance of 4,790,076 shares of common stock from private placement		48	5,762			5,810
Issuance of warrants in connection with private placement of notes payable	—	—	307	—	—	307
Loan payment from stockholder	—	—	—	168	—	168
Non-employee stock compensation	—	—	6	—	—	6
Employee stock compensation	—	—	804	—	—	804
Net loss	—	—	—	—	(16,611)	(16,611)
Balances, December 31, 2006	**$ —**	**$ 933**	**$145,827**	**$ —**	**$ (153,062)**	**$ (6,302)**

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2006	2005	2004
		(in thousands)	
Operating activities:			
Net loss	$ (16,611)	$ (15,215)	$ (5,514)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	97	57	176
Stock-based compensation	810	14	96
Gain on sale of asset	—	(4)	(4,616)
Amortization of deferred debt issuance costs	809	—	1
Accretion of debt discount	798	—	—
Changes in:			
Inventories, prepaid expenses and other current assets	(697)	(9)	21
Accrued interest	699	—	20
Accounts payable	(1,564)	1,367	(398)
Accrued liabilities	(786)	380	142
Accrued compensation and related expense, and deferred rent	216	46	49
Net cash used in operating activities	(16,229)	(13,364)	(10,023)
Investing activities:			
Purchases of property and equipment	(322)	(236)	(13)
Proceeds from sale of asset	—	4	—
Restricted cash decrease (increase)	—	95	(170)
Net cash used in investing activities	(322)	(137)	(183)
Financing activities:			
Payment of capital lease obligation	(10)	—	(13)
Note payment received from stockholder	168	19	21
Payments of notes payable to related parties	—	(73)	(604)
Payment of convertible note payable	—	—	(17)
Issuance costs related to 2004 equity private placement	—	(262)	—
Issuance of short-term notes payable, net of issuance costs	1,783	3,815	—
Issuance of common stock from exercise of options, employee stock Purchase plan and warrants, net of issuance costs	5,759	536	14
Issuance of common stock from private placement, net of issuance costs	5,810	8,142	15,111
Net cash provided by financing activities	13,510	12,177	14,512
Net decrease in cash and cash equivalents	(3,041)	(1,324)	4,306
Cash and cash equivalents, beginning of year	4,027	5,351	1,045
Unrestricted cash and cash equivalents, end of year	$ 986	$ 4,027	$ 5,351
Supplemental cash flow information:			
Cash paid for interest	$ 16	$ 2	$ 11
Taxes paid	$ 1	$ 1	$ 1
Non cash investing and financing activities:			
Conversion of debentures and interest payable to common stock	$ —	$ —	$ 73
Issuance of warrants to lenders in connection with note payable	$ 307	$ 491	$ —
Issuance of warrants to placement agent in connection with notes payable	$ —	$ 129	$ —
Acquisition of property and equipment through capital lease	$ 71	$ —	$ —

See accompanying notes to consolidated financial statements.

INSITE VISION INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2006

1. Summary of Significant Accounting Policies

Basis of Presentation. The accompanying consolidated financial statements include the accounts of InSite Vision, Ophthalmic Solutions, Inc., its wholly-owned subsidiary and its wholly-owned United Kingdom subsidiary, InSite Vision Limited. InSite Vision Incorporated (the "Company" or "InSite Vision") operated in one segment and is focused on ophthalmic genetics and developing ophthalmic drugs and ophthalmic drug delivery systems. All intercompany accounts and transactions have been eliminated.

The Company's consolidated financial statements have been presented on a basis that contemplates the realization of assets and the satisfaction of liabilities in the normal course of business and assumes the Company will continue as a going concern. Except for 1999, the Company has incurred losses since its inception, including a net loss of $16.6 million for the year ended December 31, 2006, and the Company expects to incur substantial additional losses, including additional development costs, costs related to clinical trials and manufacturing expenses. The Company has incurred negative cash flows from operations since inception, including net cash used in operations of $16.2 million for the year ended December 31, 2006. As of December 31, 2006, the Company had an accumulated deficit of $153.1 million and a cash and cash equivalents balance of $1.0 million. In these circumstances the Company believes it may not have enough cash to meet its various cash needs for fiscal 2007 unless the Company is able to obtain additional cash from reaching a milestone related to a licensing agreement (see Note 13, Subsequent Events), sales of debt or equity securities, new license or collaborative agreements or exercise of outstanding warrants. There is no assurance that the milestone will be reached or additional funds from sales of equity or debt securities or from license or collaborative agreements will be available for the Company to finance its operations on acceptable terms, if at all. If the Company cannot obtain such additional financing when required, management would likely have to cease operations and liquidate the Company's assets. These conditions raise substantial doubt about the Company's ability to continue as a going concern. The financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

Any person considering an investment in the Company's securities is urged to consider the risk that the Company will cease operations at or around the end of June 2007 if additional funding is not obtained. All of the statements set forth in this report are qualified by reference to those facts.

Reclassifications

In 2006, the Company changed its classification of patent costs to be a selling, general and administrative expense, which had previously been classified as a research and development expense. This is consistent with Statement of Financial Accounting Standard ("SFAS") No. 2 on Research and Development costs. SFAS No. 2 requires that research and development costs exclude legal work in connection with patent applications, litigation and the sale or licensing of patents. The Company made the change to better reflect the expenses incurred related to active research and development activities as legal expenses which are more administrative in nature and accordingly should be charged to selling, general and administrative expense. The impact of this change on the Company's previously reported research and development and selling, general and administrative expenses in the years ended December 31, 2005 and 2004 is as follows:

	Year Ended December 31, 2005	Year Ended December 31, 2004
	(in thousands)	
Research and development as previously reported	$ 11,321	$ 7,273
Reclassification of patent expense	(631)	(485)
Research and development	$ 10,690	$ 6,788
Selling, general and administrative as previously reported	$ 3,879	$ 3,341
Reclassification of patent expense	631	485
Selling, general and administrative	$ 4,510	$ 3,826

1. Summary of Significant Accounting Policies – (continued)

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

Accounting Policies and Use of Estimates

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

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

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

Prepaid expenses and other current assets. At December 31, 2006, prepaid expenses included a receivable from the FDA of the $767,000. This receivable represents the filing fee the Company paid in June 2006 when if filed its AzaSite New Drug Application. The FDA subsequently determined the fee would be waived and refunded to the Company.

Inventory. The Company's inventories are stated at the lower of cost or market. The cost of inventory is based on the first-in first-out method. If the cost of inventory exceeds the expected market value a provision is recorded for the difference between cost and market. At December 31, 2005, the Company's inventories solely consisted of OcuGene kits which are considered finished goods.

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. The Company's policy is to write-off our fully depreciated assets. Depreciation and amortization expense for the years ended December 31, 2006, 2005 and 2004 were $97,000, $57,000 and $176,000, respectively.

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

The costs of repairs and maintenance are expensed as incurred.

Revenue Recognition. The Company recognizes up-front fees over the expected term of the related research and development services using the straight-line method. When changes in the expected term of ongoing services are identified, the amortization period for the remaining fees is appropriately modified.

Revenue related to performance milestones is recognized when the milestone is achieved based on the terms set forth in the related agreements.

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

1. Summary of Significant Accounting Policies – (continued)

The Company recognizes cost reimbursements as contract and other revenue in accordance with EITF 01-14, Income Statement Characterization of Reimbursement for "Out of Pocket" Expenses Incurred. Such cost reimbursements are recognized when the fee is fixed or determinable and collectibility is reasonably assured.

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

Revenue related to the sales of the Company's product, the OcuGene glaucoma genetic test, is recognized when all related services have been rendered and collectibility is reasonably assured. Any revenue in connection with the Company's asset purchase agreement with Bausch & Lomb was recognized over the contract period. See Note 2, "Sale of Assets and Licenses: for further discussion on the Bausch & Lomb agreement.

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

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

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

Advertising. Advertising costs are expensed as incurred. Advertising expenses for the periods ended December 31, 2006, 2005 and 2004 were not significant.

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

Effective January 1, 2006, the Company adopted the provisions of Statement of Financial Accounting Standards ("SFAS") No. 123 (revised 2004) "Share-Based Payment" ("SFAS No. 123 (R)"). SFAS No. 123 (R) establishes accounting for stock-based awards exchanged for employee services. Accordingly, stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as expense over the requisite service period. All of the Company's stock compensation is accounted for as an equity instrument. The Company previously applied Accounting Principles Board ("APB") Opinion No. 25, "Accounting for Stock Issued to Employees," and related interpretations and provided the required pro forma disclosures of SFAS No. 123, "Accounting for Stock-Based Compensation". See Note 10, "Employee Stock-Based Compensation" for further discussion of employee stock-based compensation.

Accounting for Stock Options and Warrants Exchanged for Services. The Company issues stock options and warrants to consultants of the Company in exchange for services. The Company has valued these options and warrants using the Black-Scholes option pricing model in accordance with the Emerging Issues Task Force (EITF) Consensus No. 96-18, "Accounting for Equity Investments that are Issued to Other Than Employees for Acquiring or in Conjunction with Selling Goods, or Services," at each reporting period and has recorded charges to operations over the vesting periods of the individual stock options or warrants. Such charges amounted to approximately $6,000, $14,000 and $96,000 in 2006, 2005 and 2004, respectively.

Net Loss per Share. Basic and diluted net loss per share information for all periods is presented under the requirement of SFAS No. 128, "Earnings per Share." Basic earnings per share has been computed using the weighted-average number of common shares outstanding during the period. Dilutive earnings per share is computed

1. Summary of Significant Accounting Policies – (continued)

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, warrants and convertible securities. Potentially dilutive securities have been excluded from the computation of diluted net loss per share in 2006, 2005 and 2004 as their inclusion would be antidilutive.

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

	2006	2005	2004
	(in thousands, except per share amounts)		
Numerator:			
Net loss	$(16,611)	$(15,215)	$ (5,514)
Denominator:			
Denominator for basic and diluted loss per share – weighted-average common shares outstanding	88,339	72,647	47,984
Basic and diluted net loss per share	$ (0.19)	$ (0.21)	$ (0.11)

Due to the loss applicable to common stockholders, loss per share for 2006, 2005 and 2004 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, 2006, 2005 and 2004, 23,412,320, 30,253,869 and 21,646,284 options and warrants were excluded from the calculation of diluted earnings per share because the effect was anti-dilutive.

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

Key Suppliers. The Company is dependent on single or limited source suppliers for certain materials used in its research and development 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 efforts.

Income Taxes. The Company accounts for income taxes under an asset and liability approach that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements or the Company's tax returns. In estimating future tax consequences, the Company generally considers all expected future events other than enactments and changes in the tax law or rates. A deferred tax valuation allowance is provided for deferred tax assets when it is determined that it is more likely than not that amounts will not be recovered.

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

Recent Accounting Pronouncements. In February 2006, the FASB issued Statement of Financial *Accounting Standards No. 155, Accounting for Certain Hybrid Financial Instruments — an amendment of FASB Statements No. 133 and 140* (SFAS No. 155). SFAS No. 155 permits an entity to measure at fair value any financial instrument that contains an embedded derivative that otherwise would require bifurcation. This statement is effective for all financial instruments acquired, issued, or subject to a remeasurement event occurring after the beginning of an entity's first fiscal year that begins after September 15, 2006, which is the Company's fiscal year 2007. The Company does not expect the adoption of SFAS No. 155 to have a material impact on its consolidated financial statements.

In June 2006, the FASB issued FASB Interpretation No. (FIN) 48, *Accounting for Uncertainty in Income Taxes — An Interpretation of FASB Statement No. 109* (FIN48), which prescribes a recognition threshold and

1. Summary of Significant Accounting Policies – (continued)

measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 will be effective for fiscal years beginning after December 15, 2006, which is the Company's fiscal year 2007. The Company is currently in the process of evaluating the potential impact of adopting FIN 48 on its consolidated financial statements.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 157, *Fair Value Measurements* (SFAS No. 157), which defines fair value, establishes a framework for measuring fair value under GAAP, and expands disclosures about fair value measurements. SFAS No. 157 will be effective for fiscal years beginning after November 15, 2007, which is the Company's fiscal year 2008. The Company has not yet evaluated the potential impact of adopting SFAS No. 157 on its consolidated financial statements.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 158, *Employers' Accounting for Pensions and Other Postretirement Benefits* (SFAS No. 158). SFAS No. 158 requires employers to recognize on their balance sheet an asset or liability equal to the over or under-funded benefit obligation of each defined benefit pension and other postretirement plan and to recognize as a component of other comprehensive income, net of tax, the gains or losses and prior service costs or credits that arise during the period but are not recognized as components of net periodic benefit cost. Amounts recognized in accumulated other comprehensive income, including the gains or losses, prior service costs or credits, and the transition asset or obligation remaining from the initial application of (i) FASB Statement No. 87, *Employers' Accounting for Pensions* and (ii) FASB Statement No. 106, *Employers' Accounting for Postretirement Benefits Other Than Pensions*, are adjusted as they are subsequently recognized as components of net periodic benefit cost pursuant to the recognition and amortization provisions of those statements. This change in balance sheet reporting is effective for fiscal years ending after December 15, 2006 for public companies, which is the Company's fiscal year 2006. SFAS No. 158 also eliminates the ability to use an early measurement date, commencing with fiscal years ending after December 15, 2008, which is the Company's fiscal year 2008. The Company adopted the balance sheet reporting provisions of SFAS No. 158 in the Company's 2006 fourth fiscal quarter. Adoption of SFAS 158 did not have a material impact on our December 31, 2006 consolidated financial statements.

In September 2006, the SEC issued Staff Accounting Bulletin No. 108 ("SAB 108"), "Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements." SAB 108 is effective for fiscal years ending on or after November 15, 2006 and addresses how financial statement errors should be considered from a materiality perspective and corrected. The literature provides interpretive guidance on how the effects of the carryover or reversal of prior year misstatements should be considered in quantifying a current year misstatement. Historically there have been two common approaches used to quantify such errors: (i) the "rollover" approach, which quantifies the error as the amount by which the current year income statement is misstated, and (ii) the "iron curtain" approach, which quantifies the error as the cumulative amount by which the current year balance sheet is misstated. The SEC Staff believes that companies should quantify errors using both approaches and evaluate whether either of these approaches results in quantifying a misstatement that, when all relevant quantitative and qualitative factors are considered, is material. The Company adopted the provisions of SAB 108 in the Company's 2006 fourth fiscal quarter and it had no impact on its consolidated financial statements.

In February 2007, the FASB issued FASB Statement No. 159, "The Fair Value Option for Financial Assets and Financial Liabilities — Including an amendment of FASB Statement No. 115" ("SFAS 159"). SFAS 159 creates a "fair value option" under which an entity may elect to record certain financial assets or liabilities at fair value upon their initial recognition. Subsequent changes in fair value would be recognized in earnings as those changes occur. The election of the fair value option would be made on a contract-by contract basis and would need to be supported by concurrent documentation or a preexisting documented policy. SFAS 159 requires an entity to separately disclose the fair value of these items on the balance sheet or in the footnotes to the financial statements and to provide information that would allow the financial statement user to understand the impact on earnings from changes in the fair value. SFAS 159 is effective for us beginning with fiscal year 2008. The Company is currently evaluating the impact that the adoption of SFAS 159 will have on its consolidated financial statements.

2. Sale of Assets and Licenses

In December 2003, the Company entered into agreements with Bausch & Lomb Incorporated, or Bausch & Lomb, in which the Company sold the assets related to its ISV-403 product candidate, for the treatment of ocular bacterial infections, and licensed certain DuraSite patents for use in the ISV-403 product candidate. Bausch & Lomb made a payment to the Company of $1.5 million, surrendered 4,000 shares of Series A-1 Preferred Stock and the related accumulated dividends, and will pay the Company royalties on future sales, if any. The Company had no carrying value related to the ISV-403 assets as all costs of development were expensed as incurred. Additionally, the Company agreed to provide certain contracted services to Bausch & Lomb for a period beginning in November 2003 through June 2004, for which the Company was paid an additional amount. The license and stock purchase agreements the Company entered into with Bausch & Lomb in August 2002 related to the ISV-403 product candidate were terminated.

In accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition in Financial Statements*, the Company recognized $5.8 million of gain on sale of assets, representing the cash received of $1.5 million and the value of the Series A-1 Preferred Stock surrendered of $4.3 million, on a straight-line basis over the seven month period for which contract services were provided. Correspondingly, in 2003 the Company recognized $1.2 million of gain from the sale of assets and recognized the remaining gain from the sale of assets of $4.6 million in 2004.

3. Restricted Cash

In December 2005, the Company reserved approximately $75,000 related to a letter of credit issued as collateral for a capital lease for a telephone system which was to be installed and initiated in the first quarter of 2006.

In 2004 the Company received proceeds totaling $170,000 from the sale of shares obtained from the demutualization of an insurance company, which had provided health benefits to the Company's employees. During 2005 these proceeds were used for the payment of health insurance benefits for the employees, no amounts remained outstanding as of December 31, 2005.

4. Short-term Notes Payable to Related Parties, Unsecured

In August, September and November 2003, the Company issued a total of $188,000 in a series of short-term unsecured notes payable to members of the Board of Directors, senior management and other employees of the Company for cash. As of December 31, 2006, $35,000 remains outstanding. These notes bear interest at a rate of two percent (2%). In February 2007 these notes were repaid in full.

5. Short-term Notes Payable to Related Parties, Secured

In July and August 2003, the Company issued $500,000 in short-term Senior Secured Notes payable to an officer who is also a member of the Board of Directors and to an affiliate of a member of senior management for cash. In November 2003, the Company increased one of the short-term Senior Secured Notes by $20,000 after receipt of cash. These notes bear interest at a rate of between five and one-half percent (5.5%) and twelve percent (12%), were due between September 30, 2003 and October 15, 2003 and, in combination with the notes described in Note 6, are secured by a lien on substantially all of the assets of the Company, including the Company's intellectual property, other than certain other equipment secured by the lessor of such equipment. Prior to September 30, 2003 the due dates of these notes were extended to between November 15, 2003 and December 31, 2003. Subsequently, the due dates were further extended to January 15, 2004 and March 31, 2004. In January 2004, the Company repaid $120,000 of these Senior Secured Notes and the related accrued interest. In July 2004, the Company repaid $169,000 of these Senior Secured Notes and the related accrued interest. In December 2005 the due date of the remaining note was further extended to March 31, 2007. The Company had $231,000 of one of these short-term secured notes payable to related parties outstanding at December 31, 2006. In February 2007 these notes were repaid in full.

6. Short-term Notes Payable, Secured

In December 2005, the Company issued a total of $4,300,000 of short-term Senior Secured Notes payable and warrants to purchase 860,000 shares of Common Stock at an exercise price of $0.82 per share. The Company also issued warrants to purchase 200,000 shares of Common Stock at an exercise price of $0.82 per share to the placement agent engaged for such financing. These warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 4.30%, volatility of 103% and an expected life of 5 years. The relative fair value model was then applied to the Black-Scholes valuation of the warrants issued to the note holders resulting in the recording of a debt discount of $491,000 which will be amortized over the term of the notes. The Black-Scholes model resulted in a deferred debt issue cost of $129,000 for the warrants issued to the placement agent which will be amortized over the term of the notes.

In January 2006, the Company issued an additional $2,000,000 short-term Senior Secured Notes payable and warrants to purchase 400,000 shares of Common Stock at an exercise price of $0.82 per share. These warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 4.30%, volatility of 103% and an expected life of 5 years. The relative fair value model was then applied to the Black-Scholes valuation of the warrants issued to the note holders resulting in the recording of a debt discount of $307,000 which will be amortized over the term of the notes.

These notes, and the Senior Secured Note described in Note 5, are secured by a lien on all of the assets of the Company, including the Company's intellectual property. These notes bear interest at a rate of ten percent (10%) and had an original maturity date of June 30, 2006, but were extended for an additional six months at an interest rate of twelve percent (12%). In December 2006 the due date was further extended to February 15, 2007. Payments of principal and interest under the Notes are due in one lump sum upon the earlier of the applicable maturity date or an "Event of Acceleration" under the Notes. In February 2007 these notes were repaid in full.

The weighted average interest rate for the unsecured and secured notes payable was 11.7% and 9.7% at December 31, 2006 and 2005, respectively.

7. Commitments and Contingencies

At December 31, 2006, the Company had purchase commitments and contractual obligations of approximately $0.9 million, primarily related to its insurance coverage, minimum license fees and consultants. These purchase commitments and contractual obligations are reflected in the Company's financial statements once the related goods or services have been received or payments related to the obligations become due.

Capital lease obligations represent the present value of future rental payments under capital lease agreements for telephones and telephone equipment. The original cost and accumulated amortization on the equipment under capital leases was $71,000 and $7,000, respectively, at December 31, 2006.

7. Commitments and Contingencies – (continued)

Future minimum payments under capital leases are as follows:

Year Ending December 31,	Capital Leases
2007	$ 17,662
2008	17,662
2009	17,661
2010	17,661
2011	4,750
Total minimum lease payments	75,396
Amount representing interest	(14,241)
Present value of net minimum lease payments	61,155
Current portion	(12,134)
Long-term portion	$ 49,021

The Company its operations from leased facilities in Alameda, California under non-cancelable operating lease agreements that expire in 2013. Lease payments include rent and the Company's pro-rata share of operation expenses. For accounting purposes, the Company is amortizing all rent payments ratably over the life of the lease. Future minimum lease payments under the terms of the amended lease agreement dated November 28, 2006 and a reconciliation of rent expense to rent paid is in the table below. Rent expense was $706,000, $719,000, and $719,000 for 2006, 2005 and 2004, respectively.

		Facility Lease	
Year Ending December 31,	Cash Payments Required	Expense	Deferred Rent
2006	$ 45,244	$ 50,945	$ (5,701)
2007	559,300	611,356	(52,056)
2008	575,677	611,356	(35,679)
2009	594,319	611,356	(17,037)
2010	610,696	611,356	(660)
2011	629,337	611,356	17,981
Thereafter	1,315,864	1,222,712	93,152
Total minimum lease payments	$ 4,330,437	$4,330,437	

8. Income Taxes

Due to the company's history of net operating losses, there is no provision for income taxes for the years ended December 31, 2006, 2005 and 2004.

8. Income Taxes – (continued)

Significant components of the Company's deferred tax assets for federal and state income taxes as of December 31, 2006 and 2005 are as follows (in thousands):

	2006	2005
Deferred tax assets:		
Net operating loss carryforwards	$ 40,614	$ 35,503
Tax credit carryforwards	6,456	6,038
Capitalized research and development	12,263	11,016
Depreciation	398	453
Other	95	192
Total deferred tax assets	59,826	53,202
Valuation allowance	(59,826)	(53,202)
Net deferred tax assets	$ —	$ —

The valuation allowance increased by $6.6 million, $4.4 million, and $857,000 during the years ended December 31, 2006, 2005 and 2004, respectively.

At December 31, 2006, the Company had net operating loss carryforwards for federal income tax purposes of approximately $106.7 million, which expire in the years 2006 through 2025 and federal tax credits of approximately $3.4 million, which expire in the years 2006 through 2025. At December 31, 2006, the Company also has net operating loss carryforwards for state income tax purposes of approximately $72.1 million which expire in the years 2006 through 2015, and state research and development tax credits of approximately and $3.0 million which carryforward indefinitely.

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

9. Common Stockholders' Equity (Deficit)

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

Warrants Issued as Part of:	Exercise Price	Net Cash Received	Fees Incurred	Warrants Exercised	Shares of Common Stock Issued
March 2004 private placement	$ 0.75	$5,256,000	$162,000	7,223,763	7,223,763
Placement agent warrants related to the March 2004 private placement, cashless exercise	$ 0.55	—	—	29,077	17,719
May 2005 private placement	$0.6325	345,000	—	545,451	545,451
May 2005 private placement, cashless exercise	$0.6325	—	—	436,361	274,074
Legal settlement	$ 0.50	—	—	922,800	565,125
2003 services provided	$ 0.50	25,000	—	50,000	50,000
Total		$5,626,000	$162,000	9,207,452	8,676,132

9. Common Stockholders' Equity (Deficit) – (continued)

In 2006, the Company also received approximately $133,000 from the exercise of options to purchase 136,257 shares of Common Stock issued to employees and the purchase of 67,663 shares under the Company's employee stock purchase plan.

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

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

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

In 2005, the Company received approximately $298,000, net of approximately $9,000 of fees, from the exercise of warrants to purchase 410,206 shares of Common Stock issued as part of the March 2004 private placement. In December 2005, the Company received approximately $145,000 from the exercise of warrants to purchase 268,519 shares of Common Stock issued in December 2003. In January 2005, the Company received approximately $50,000 from the exercise of warrants to purchase 125,000 shares of Common Stock issued in November 2003. In August 2005, the Company received approximately $10,000 from the exercise of an employee stock option to purchase 25,000 shares of Common Stock.

On June 28, 2004, the Company converted a $50,000 short-term note payable issued June 30, 2003, and the related accumulated interest payable, by issuing 105,951 shares of Common Stock at a price of $0.50 per share.

On March 26, 2004, the Company received, net of issuance costs of $0.3 million, approximately $1.7 million from the initial closing of a private placement totaling $16.5 million. At the initial closing, the Company issued 3,880,000 shares of Common Stock and warrants to purchase 1,940,000 shares of Common Stock at an exercise price of $0.75 per share. These warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 2.64%, volatility of 1.0679 and an expected life of 5 years, resulting in the recording of a stock issue cost of $1.5 million. In April 2004, the warrant was partially exercised for 2,940 shares of Common Stock.

On June 14, 2004, the Company received, net of issuance costs of $1.1 million, approximately $13.4 million from the final closing of the March 2004 private placement. At the final closing the Company issued 29,120,000 shares of Common Stock and warrants to purchase 14,560,000 shares of Common Stock at an exercise price of

9. Common Stockholders' Equity (Deficit) – (continued)

$0.75 per share. The Company also issued warrants to purchase 750,000 shares of Common Stock at an exercise price of $0.55 per share to the placement agent engaged for such financing. These warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 3.92%, volatility of 1.0662 and an expected life of 5 years, resulting in the recording of a stock issue cost of $8.0 million for the warrants issued to the investors in the private placement and $427,000 for the warrants issued to the placement agent.

10. Employee Stock-based Compensation

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

Impact of the Adoption of SFAS 123 (R)

The Company elected to adopt the modified prospective application method as provided by SFAS No. 123(R). The effect of recording stock-based compensation for the year ended December 31, 2006 was as follows (in thousands, except per share data):

Stock-Based Compensation Expense by Type of Award:	Year Ended December 31, 2006
Employee stock options	$ 780
Employee stock purchase plan	24
Non-employee stock options	6
Total stock-based compensation	810
Tax effect on stock-based compensation	—
Total stock-based compensation expense	$ 810
Impact on net loss per share	$ (0.01)

As of January 1, 2006, the Company had an unrecorded deferred stock-based compensation balance related to stock options of approximately $1.4 million before estimated forfeitures. In the Company's pro forma disclosures prior to the adoption of SFAS No. 123 (R), the Company accounted for forfeitures upon occurrence. SFAS No. 123 (R) requires forfeitures to be estimated at the time of grant and revised if necessary in subsequent periods if actual forfeitures differ from those estimates. 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.

During the year ended December 31, 2006, the Company granted options to purchase 1,628,200 shares of Common Stock with an estimated total grant date fair value of $1.6 million. Of the $1.6 million, the Company estimated the stock-based compensation for awards not expected to vest was $0.3 million.

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

10. Employee Stock-based Compensation – (continued)

Valuation assumptions

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

	Year Ended December 31, 2006
Risk-free interest rate	4.62%
Expected term (years)	5
Expected dividends	0.0%
Volatility	78.0%

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

Equity Incentive Program

The Company currently grants options under a stock option plan adopted in 1994 and amended thereafter (the "1994 Plan"), that allows for the granting of non-qualified stock options, incentive stock options and stock purchase rights to the Company's employees, directors, and consultants. At December 31, 2006, a total of 7,229,422 shares of Common Stock were reserved under the 1994 Stock Plan for issuance upon the exercise of options or by direct sale to employees, including officers, directors and consultants. Options granted under the plan expire 10 years from the date of grant and become exercisable at such times and under such conditions as determined by the Company's Board of Directors (generally with 25% vesting after one year and the balance vesting on a daily basis over the next three years of service). Upon termination, unexercised options will generally expire at the end of 60 days. No stock purchase rights or incentive stock options have been granted under the 1994 Plan to date. Under the terms of the 1994 Stock Plan, there is an automatic share increase feature pursuant to which the number of shares available for issuance is automatically increased on the first trading day in January each calendar year, beginning with calendar year 2002 and continuing over the term of the Plan by an amount equal to 2% of the total number of shares of common stock outstanding on the last trading day in December in the immediately preceding calendar year. A summary of activity under the 1994 Plan is as follows:

10. Employee Stock-based Compensation – (continued)

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Balances at December 31, 2003	3,051,329	$ 1.85		
Granted	968,000	0.77		
Exercised	(8,784)	0.70		
Forfeited	(174,809)	1.86		
Balances at December 31, 2004	3,835,736	$ 1.58	6.28	$ 326
Granted	2,175,000	0.65		
Exercised	(25,000)	0.41		
Forfeited	(430,746)	2.40		
Outstanding at December 31, 2005	5,554,990	$ 1.15	7.24	$ 639
Granted	1,628,200	1.52		
Exercised	(136,257)	0.68		
Forfeited	(464,055)	2.01		
Balances at December 31, 2006	6,582,878	$ 1.19	7.08	$ 3,597
Options vested and exercisable and expected to be exercisable at December 31, 2006	6,263,406	$ 1.20	6.99	$ 3,463
Options vested and exercisable at December 31, 2006	3,720,567	$ 1.25	5.80	$ 2,370

At December 31, 2006, the Company had 646,544 shares of Common Stock available for grant or issuance under the 1994 Plan. The weighted average grant date fair value of options granted during the years ended December 31, 2006, 2005 and 2004 were $1.00, $0.65 and $0.77, respectively. The total intrinsic value of options exercised during the years ended December 31, 2006 and 2005 were $157,000 and $2,000, respectively.

The following table summarizes information concerning outstanding and exercisable options as of December 31, 2006:

	Options Outstanding			Options Vested and Exercisable	
		Weighted Average			
Range of Exercise Prices	Number Outstanding	Contractual Life	Exercise Price	Number Exercisable	Weighted Average Exercise Price
$0.41 – $0.60	282,500	6.98	$ 0.41	256,372	$ 0.41
$0.63 – $0.63	2,026,836	8.29	0.63	1,043,268	0.63
$0.64 – $1.13	1,912,592	6.10	0.87	1,628,177	0.89
$1.20 – $6.23	2,360,950	6.84	2.03	792,750	3.06
	6,582,878	7.08	$ 1.19	3,720,567	$ 1.25

At December 31, 2005 and 2004 options to purchase 3,173,607 and 2,715,213 shares of Common Stock were exercisable at weighted average exercise prices of $1.51 and $1.91 per share, respectively.

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

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

10. Employee Stock-based Compensation – (continued)

The fair value for these options was estimated at the date of grant using a Black-Scholes option pricing model with the following weighted-average assumptions for 2005 and 2004, respectively: risk-free interest rates ranging from 0.89% to 4.44%; volatility factors for the expected market price of our common stock of 103% and 105%; expected life of 4 years; and an expected dividend rate of 0%.

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

	Year Ended December 31,	
	2005	2004
Net loss – as reported	$ (15,215)	$ (5,514)
Deduct: Total stock-based employee compensation expense determined under fair value method for all awards	(524)	(372)
Net loss – pro forma	$ (15,739)	$ (5,886)
Loss per share:		
Basic and diluted-as reported	$ (0.21)	$ (0.11)
Basic and diluted-pro forma	$ (0.22)	$ (0.12)

Pursuant to the terms of the 1994 Stock Plan, generally each non-employee director who is newly elected or appointed after October 25, 1993, is granted an option to purchase 10,000 shares of Common Stock at a price per share equal to the fair market value of the Common Stock on the grant date. Each continuing non-employee director also receives an annual grant of an option to purchase 10,000 shares. Such options vest one year after the grant date.

In June 2002, the Company's stockholders approved a series of amendments to the Company's 1994 Stock Option Plan, or the 1994 Plan, including (i) increasing the maximum number of shares of Common Stock issuable to any one person under the 1994 Plan over the term of the 1994 Plan by 400,000 shares so that the limit is increased from 850,000 shares to 1,250,000 shares and (ii) extending the term of the 1994 Plan by an additional 5 years so that the expiration date is extended from July 27, 2003 to July 27, 2008.

The Company granted stock options to non-employees which resulted in compensation expense of $6,000, $14,000 and $65,000 in 2006, 2005 and 2004, respectively.

Employee Stock Purchase Plan

The Company currently has an employee stock purchase plan, adopted in 1994 and amended thereafter (the "Purchase Plan"). The Purchase Plan allows eligible employees to purchase Common Stock at 85% of the lower of the fair market value of the Common Stock on the subscription date or the fair market value on the purchase date. The offering period under the Purchase Plan is currently 24 months, and the purchase price is established during each new offering period. Purchases are limited to 15% of each employee's eligible compensation and subject to certain Internal Revenue Service restrictions. All of the Company's employees are eligible to participate in the Purchase Plan after certain service periods are met. In June 2002, the Company's stockholders approved a series of amendments to the Company's Purchase Plan, including (i) increasing by 100,000 the total number of shares of the Company's Common Stock authorized for issuance under the Purchase Plan, (ii) extending the term of the Purchase Plan by an additional 5 years so that the expiration date is extended from December 31, 2003 to December 31, 2008, and (iii) implementing an automatic share increase feature pursuant to which the number of shares available for issuance under the Purchase Plan is automatically increased on the first trading day in January each calendar year, beginning with calendar year 2003 and continuing over the remaining term of the Purchase Plan, as extended, by an amount equal to 0.5% of the total number of shares of Common Stock outstanding on the last trading day in

10. Employee Stock-based Compensation – (continued)

December in the immediately preceding calendar year, but in no event will any such annual increase exceed 125,000 shares. As of December 31, 2006, 605,959 shares were reserved for issuance under the Purchase Plan.

The fair value of shares purchased under the Purchase Plan is estimated using the Black-Scholes option valuation model and the graded-vesting method with the following weighted average assumptions for the year ended December 31, 2006: risk-free interest rate of 5.1%; volatility factor of 78.2%; and an expected life of 1.5 years. During the year ended December 31, 2006, the compensation cost in connection with the Purchase Plan was $24,000 and 67,663 shares were issued under the Purchase Plan. As of December 31, 2006, the unrecorded deferred stock-based compensation balance related to the Purchase Plan was $8,000 and will be recognized over an estimated weighted average amortization period of 1.0 years. The weighted average grant date fair value of the Purchase Plan shares issued during 2006, 2005 and 2004 was $0.60, $0.55 and $0.55, respectively.

11. Notes Receivable from Stockholder

In May 2000, the Company issued loans to Dr. Chandrasekaran, the Company's President, Chief Executive Officer, Chief Financial Officer and Chairman of the Board, related to his exercise of 126,667 options to acquire common stock. In May 2001, the terms on the loans were extended from 4 years to 5 years. In 2005 and 2004, Dr. Chandrasekaran made principal and interest payments of approximately $19,000 and $21,000, respectively. The loans are full recourse and bear interest at 7% per annum. Interest payments are due semi-annually and principal payments are due annually. While the 126,667 shares of common stock issued secure the loans, the Company is not limited to these shares to satisfy the loan. In January 2006, these notes were repaid in full.

12. Legal Proceedings

On July 8, 2004, Bristol Investment Group, or Bristol, filed with the American Arbitration Association a demand for arbitration against us seeking cash compensation and warrants based on a letter agreement dated January 28, 2003 pursuant to which Bristol was engaged as a non-exclusive placement agent of investment capital for the Company. On October 6, 2005 the arbitrator issued the final award in favor of Bristol, ruling that Bristol is entitled to recover $249,925, plus interest, attorneys' and other fees, plus Bristol has the right to purchase for $922.80 a five-year, net-exerciseable warrant to purchase 922,800 shares of our common stock at an exercise price of $0.50 per share. The Company recorded the attorneys' and other fees in selling, general and administrative expenses and the remainder of which was recorded as a stock issuance cost in additional paid-in-capital. The warrants were valued using a Black-Scholes option pricing model, assuming no dividend yield, with the following assumptions: risk-free interest rate of 4.18%, volatility of 1.04 and an expected life of 5 years, resulting in the recording of a stock issue cost of approximately $467,000. In January 2006, the warrants were exercised using the non-cash exercise provision in the warrant for a total of 565,125 shares of Common Stock.

On or about October 8, 2003, a former consultant filed a complaint in the Superior Court of California, County of San Francisco, against the Company, our Chief Executive Officer, Dr. Chandrasekaran, the Regents of the University of California or "Regents," and two individuals associated with Regents. The former consultant alleged that the Company breached an obligation to continue supporting his research; he also made a variety of other related claims and allegations against the Company and the other defendants. In December 2004, the parties reached a settlement resulting in a total cash payment owed to the consultant of $250,000, of which $100,000 was reimbursed by the Company's insurance carrier, and the Company issued an option to purchase 30,000 shares of Common Stock valued at $23,253. At December 31, 2004 the Company had paid $75,000 of the settlement payment owed and accrued the remainder, which was paid in 2005.

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

13. Related Party

Included in accounts payable on the balance sheet at December 31, 2006 and 2005 is $17,000 and $27,000, respectively, due to related parties for expenses incurred on behalf of the Company. See Notes 4 and 5 for discussion of related party notes payable transactions.

14. Subsequent Events

On February 15, 2007, the Company entered into a license agreement with Inspire under which the Company licensed to Inspire exclusive development and commercialization rights, under the Company's 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. The Inspire License also provides for nonexclusive licenses under the Company's DuraSite patent rights, container patent rights, Columbia patent rights and certain know-how in the same field of use as described above. The Company also grants Inspire an exclusive sublicense under the Pfizer patent rights the Company has licensed under the Pfizer License discussed below. Inspire has the right to grant sublicenses under the terms of the Inspire License.

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

The Company also entered into a trademark license agreement with Inspire on February 15, 2007 under which the Company granted to Inspire an exclusive license to the AzaSite™ trademark and domain name and a nonexclusive license to the DuraSite® trademark in connection with the commercialization of Subject Products in the Territory under the terms of the Inspire License.

The Company also entered into a supply agreement, or the Supply Agreement, with Inspire on February 15, 2007 for the active pharmaceutical ingredient azithromycin. The Company had previously entered into a third party supply agreement for the production of such active ingredient. Under the Supply Agreement, the Company agreed to supply Inspire's requirements of such active ingredient, pursuant to certain forecasting and ordering procedures.

The Company used approximately $7.3 million of the license fee it received under the Inspire License to repay its secured and unsecured short-term notes payable and the related interest.

On February 15, 2007, the Company entered into a worldwide, exclusive, royalty bearing licensing agreement with Pfizer Inc. and Pfizer Products, Inc., or collectively Pfizer, under Pfizer's patent family titled "Method of Treating Eye Infections with Azithromycin" for ocular anti-infective product candidates known as AzaSite and AzaSite Plus.

Under the Pfizer License, the Company is required to pay Pfizer a single digit royalty based on net sales of the licensed products and to use reasonable commercial efforts to seek regulatory approval for and market licensed products. 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.

15. Quarterly Results (Unaudited)

The following table is a summary of the quarterly results of operations for the years ended December 31, 2006 and 2005. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	2006				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
	(in thousands, except per share amounts)				
Revenues	$ 1	$ —	$ 1	$ —	$ 2
Cost of revenue	3	3	20	2	28
Loss from operations	(4,811)	(4,570)	(3,091)	(2,626)	(15,098)
Net loss	(5,321)	(5,129)	(3,337)	(2,824)	(16,611)
Basic and diluted net loss per share	$ (0.06)	$ (0.06)	$ (0.04)	$ (0.03)	$ (0.19)
Shares used to calculate basic and diluted net loss per share	83,756	86,848	90,301	92,868	88,339

	2005				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
Revenues	$ 1	$ 1	$ 1	$ 1	$ 4
Cost of goods	5	3	3	3	14
Loss from operations	(3,435)	(4,216)	(3,488)	(4,071)	(15,210)
Net loss	(3,438)	(4,216)	(3,488)	(4,072)	(15,215)
Basic and diluted net loss per share	$ (0.06)	$ (0.06)	$ (0.04)	$ (0.05)	$ (0.21)
Shares used to calculate basic and diluted net loss per share	62,493	70,699	78,903	79,092	72,647

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

None

Item 9A. Controls and Procedures

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

Report of Management on Internal Control Over Financial Reporting. Our management is responsible for establishing and maintaining a comprehensive system of internal control over financial reporting to provide reasonable assurance of the proper authorization of transactions, the safeguarding of assets and the reliability of the financial records. Our internal control system was designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. The system of internal control over financial reporting provides for appropriate division of responsibility and is documented by written policies and procedures that are communicated to employees. The framework upon which management relied in evaluating the effectiveness of our internal control over financial reporting was set forth in *Internal Controls — Integrated Framework* published by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on the results of our evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2006.

Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our independent registered public accounting firm, which has audited the financial statements included in Item 8 of this report, has issued an attestation report on management's assessment of our internal control over financial reporting which is included below.

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

Changes in Internal Control over Financial Reporting. There were no changes in our internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f)) during the quarter ended December 31, 2006 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Independent Registered Public Accounting Firm's Attestation Report.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of InSite Vision Incorporated

We have audited management's assessment, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting included in Item 9A, that InSite Vision Incorporated and its subsidiaries (the "Company") maintained effective internal control over financial reporting as of December 31, 2006, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the Company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, management's assessment that InSite Vision Incorporated and its subsidiaries maintained effective internal control over financial reporting as of December 31, 2006, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, InSite Vision Incorporated and its subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2006, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of InSite Vision Incorporated and its subsidiaries as of December 31, 2006 and 2005, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2006 and our report dated March 15, 2007 expressed an unqualified opinion on those consolidated financial statements and included an explanatory paragraph regarding a substantial doubt about the Company's ability to continue as a going concern.

/s/ Burr, Pilger, & Mayer LLP

Palo Alto, California
March 15, 2007

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors and Executive Officers of the Company

(a) The sections labeled "Nominees for Directors," "Board Committees and Meetings," "Audit Committee Matters," "Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" of our Proxy Statement in connection with the 2007 Annual Meeting of Stockholders are incorporated herein by reference.

(b) Information concerning our Executive Officers is set forth in Part I of this Form 10-K.

Item 11. Executive Compensation

The sections labeled "Director Compensation for 2006," "Compensation, Discussion and Analysis," "Compensation of Named Executive Officers," "Summary Compensation Table for 2006," "Grants of Plan Based Awards in 2006," "Outstanding Equity Awards at Fiscal 2006 Year End," "Option Exercises and Stock Vested in 2006," "Non-Qualified Deferred Compensation for 2006," "Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report" of our Proxy Statement in connection with the 2007 Annual Meeting of Stockholders are incorporated herein by reference.

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

The sections labeled "Equity Compensation Plans" and "Beneficial Ownership of Principal Stockholders, Directors and Management" of our Proxy Statement in connection with the 2007 Annual Meeting of Stockholders are incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions

The sections labeled "Certain Relationships and Related Persons Transactions" and "Director Independence" of our Proxy Statement in connection with the 2007 Annual Meeting of Stockholders is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Audit Fees

The section labeled "Audit Committee Matters" and "Principal Accounting Fees and Services" of our Proxy Statement in connection with the 2007 Annual Meeting of Stockholders is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a)(1) ***Financial Statements***

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

(2) ***Financial Statement Schedules***

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

(3) ***Exhibits***

See Exhibit Index on page 72 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.

INSITE VISION INCORPORATED

Dated: March 15, 2007

By: /s/ S. Kumar Chandrasekaran
S. Kumar Chandrasekaran, Ph.D.
Chairman of the Board, President,
Chief Executive Officer and
Chief Financial Officer

POWER OF ATTORNEY

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

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

Name	Capacity	Date
/s/ S. Kumar Chandrasekaran S. Kumar Chandrasekaran, Ph.D.	Chairman of the Board, President, Chief Executive Officer and Chief Financial Officer	March 15, 2007
/s/ Mitchell H. Friedlaender Mitchell H. Friedlaender, M. D.	Director	March 15, 2007
/s/ John L. Mattana John L. Mattana	Director	March 15, 2007
/s/ Jon S. Saxe Jon S. Saxe	Director	March 15, 2007
/s/ Anders P. Wiklund Anders P. Wiklund	Director	March 15, 2007

EXHIBIT INDEX

Number		Exhibit Table
3.1	1	Restated Certificate of Incorporation.
3.2	9	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	9	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	15	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	20	Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on June 3, 1994.
3.6	6	Amended and Restated Bylaws.
3.7		Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on July 20, 2000.
3.8		Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on June 1, 2004.
3.9	26	Certificate of Amendment to Restated Certificate of Incorporation as filed with the Delaware Secretary of State on October 23, 2006.
4.1		Reference is made to Exhibits 3.1 through 3.9.
10.1	10	InSite Vision Incorporated 1994 Employee Stock Purchase Plan (As amended and restated through April 17, 2000).
10.2	8HH	InSite Vision Incorporated 1994 Stock Option Plan (Amended and Restated as of June 8, 1998).
10.3	1HH	Form of InSite Vision Incorporated Notice of Grant of Stock Option and Stock Option Agreement, with Addenda.
10.4	8HH	Form of InSite Vision Incorporated Notice of Automatic Option Grant and Non-Employee Director Option Agreement.
10.6	1	Form of InSite Vision Incorporated Stock Purchase Agreement.
10.7	1	Form of InSite Vision Incorporated Employee Stock Purchase Plan Enrollment/Change Form.
10.8	2	Form of Indemnity Agreement Between the Registrant and its directors and officers.
10.9	2	Form of Employee's Proprietary Information and Inventions Agreement.
10.10	3H	License Agreement dated as of October 9, 1991 by and between the Company and CIBA Vision Corporation, as amended October 9, 1991.
10.11	3H	Letter Agreement dated February 27, 1992 by and among the Company, Columbia Laboratories, Inc. and Joseph R. Robinson, as amended October 23, 1992.
10.12	7	Facilities Lease, dated September 1, 1996, between the Registrant and Alameda Real Estate Investments.
10.13	4	Common Stock Purchase Agreement dated January 19, 1996 between the Registrant and the Investors listed on Schedule 1 thereto.
10.14	5H	ISV-205 License Agreement dated May 28, 1996 by and between the Company and CIBA Vision Ophthalmics.
10.15	5H	ToPreSite License Agreement dated May 28, 1996 by and between the Company and CIBA Vision Ophthalmics.
10.16	5H	Timolol Development Agreement dated July 18, 1996 by and between the Company and Bausch & Lomb Pharmaceuticals, Inc.

Number		Exhibit Table
10.17	5H	Stock Purchase Agreement dated July 18, 1996 by and between the Company and Bausch & Lomb Pharmaceuticals, Inc.
10.18	9H	License Agreement, dated July 1, 1997, by and between the University of Connecticut Health Center and the Company.
10.19	9H	License Agreement, dated August 19, 1997, by and between the University of Rochester and the Company.
10.20	11	Form of Stock and Warrant Purchase Agreement, dated May 1, 2000 by and among the Company and the purchasers thereto.
10.21	12	Placement Agent Agreement with Ladenburg Thalmann & Co., Inc. dated January 9, 2001.
10.22	13	Amendment No. 1 to Marina Village Office Tech Lease, dated July 20, 2001 and effective January 1, 2002.
10.23	14H	License Agreement, dated December 21, 2001 by and between the Company and The University of Connecticut Health Center.
10.24	16	Form of Promissory Notes in the aggregate principal amount of $188,500, dated between June 13, 2003 and June 30, 2003, issued by the Company to certain members of the Company's Board of Directors, senior management, and stockholders.
10.25	16	Form of Waiver and Amendment to Promissory Notes to Promissory Notes by and between the Company and the holders of the promissory Notes included as Exhibit 10.24 hereto.
10.26	18H	ISV-403 Asset Purchase Agreement, dated December 19, 2003, between the Company and Bausch & Lomb, Inc.
10.27	19	Form of Subscription Agreement, dated as of March 26, 2004, by and between the Company and the Subscribers named on the signature pages thereto.
10.28	19	Form of Class A Warrants.
10.29	19	Form of Class B Warrants.
10.30	19	Form of Placement Warrant.
10.31	19	Placement Agent Agreement, dated as of February 12, 2004, by and between the Company and Paramount Capital, Inc.
10.32	20	Form of Subscription Agreement, dated on or about May 26, 2005 by and between the Company and the Subscribers named on the signature pages thereto.
10.33	20	Form of Warrant for the purchase of shares of Common Stock of the Company.
10.34	20	Form of Placement Agent Warrant, dated as of May 9, 2005.
10.35	20	Placement Agent Agreement, dated as of February 24, 2005, by and between the Company and Paramount BioCapital, Inc.
10.36	21	Warrant, dated as of October 10, 2005, for the purchase of 922,800 shares of Common Stock of the Company.
10.37	22	Form of Subscription Agreement, dated as of December 30, 2005 by and between the Company and the Subscribers named on the signature pages thereto.
10.38	22	Form of Warrant, dated as of January 11, 2006.
10.39	22	Form of Placement Agent Warrant, dated as of January 11, 2006.
10.40	22	Form of Consent to Expand Size of Offering of Notes and Warrants, dated as of January 6, 2006.
10.41	23	Placement Agent Agreement, dated as of December 16, 2005, by and between the Company and Paramount BioCapital, Inc.
10.42	23	Amended and Restated Security Agreement, dated as of December 30, 2005, by and between the Company and The Bank of New York.

Number		Exhibit Table
10.43	23	Collateral Agency and Intercreditor Agreement, dated as of December 30, 2005, by and among the Company, S. Kumar Chandrasekaran, Ph.D. and The Bank of New York as the Collateral Agent for the holders of the Company's 2003 Senior Secured Notes and 2005 Senior Secured Notes.
10.44	23	Form of Senior Secured Note, dated as of December 30, 2005, issued to certain investors in an aggregate principal amount of $4,300,000.
10.45	23	Form of Senior Secured Note, dated as of January 11, 2006, issued to certain investors in an aggregate principal amount of $2,000,000.
10.46	23	Amended and Restated Senior Secured Note in aggregate principal amount of $231,000, dated as of December 30, 2005, issued by the Company to S. Kumar Chandrasekaran, Ph.D.
10.47	24	Form of Subscription Agreement, dated as of August 2, 2006 by and between the Company and the Subscribers named on the signature pages thereto.
10.48	24	Form of First Amendment, dated as of August 8, 2006, to Subscription Agreement dated as of August 2, 2006, by and between the Company and each of the Subscribers.
10.49	24	Form of Warrant, dated as of August 15, 2006.
10.50		Amendment No. 3 to Marina Village Office Tech Lease, dated November 28, 2006.
10.51	25	Amendment Agreement, dated as of December 22, 2006, to Senior Secured Notes dated as of December 30, 2005 and January 11, 2006 by and among the Company and each of the holders of notes.
16.1	17	Letter of Ernst & Young, LLP regarding change in certifying accountants, dated October 28, 2003.
23.1		Consent of Burr, Pilger & Mayer LLP, Independent Registered Public Accounting Firm.
31.1		Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2		Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1		Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

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1 Incorporated by reference to an exhibit in the Company's Annual Report on Form 10-K for the year ended December 31, 1993.

2 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.

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 in the Company's Annual Report on Form 10-K for the year ended December 31, 1995.

5 Incorporated by reference to an exhibit in the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 1996.

6 Incorporated by reference to an exhibit in the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2006.

7 Incorporated by reference to an exhibit in the Company's Annual Report on Form 10-K for the year ended December 31, 1996.

8 Incorporated by reference to exhibits in 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.

9 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.

10 Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-8 (Registration No. 333-43504) as filed with the Securities and Exchange Commission on August 11, 2000.

11 Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 (Registration No. 333-38266) as filed with the Securities and Exchange Commission on June 1, 2000.

12 Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 (Registration No. 333-54912) as filed with the Securities and Exchange Commission on February 2, 2001.

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 Annual Report of Form 10-K for the year ended December 31, 2001.

15 Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2002.

16 Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q/A for the quarter ended June 30, 2003.

17 Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on October 28, 2003.

18 Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on January 14, 2004.

19 Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 29, 2004.

20 Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on June 23, 2005 (File Number 333-126084).

21 Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on October 11, 2005 (File Number 001-14207).

22 Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on February 10, 2006 (File Number 333-131774).

23 Incorporated by reference to an exhibit to the Company's Annual Report on Form 10-K for the year ended December 31, 2005.

24 Incorporated by reference to an exhibit to the Company's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on October 13, 2006 (File Number 333-137994).

25 Incorporated by reference to an exhibit to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 26, 2006.

26 Incorporated by reference to an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2006.

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

HH Management contract or compensatory plan.