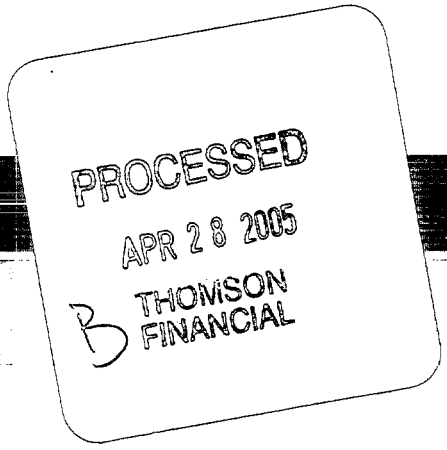
INSPIRE



2004

ANNUAL REPORT

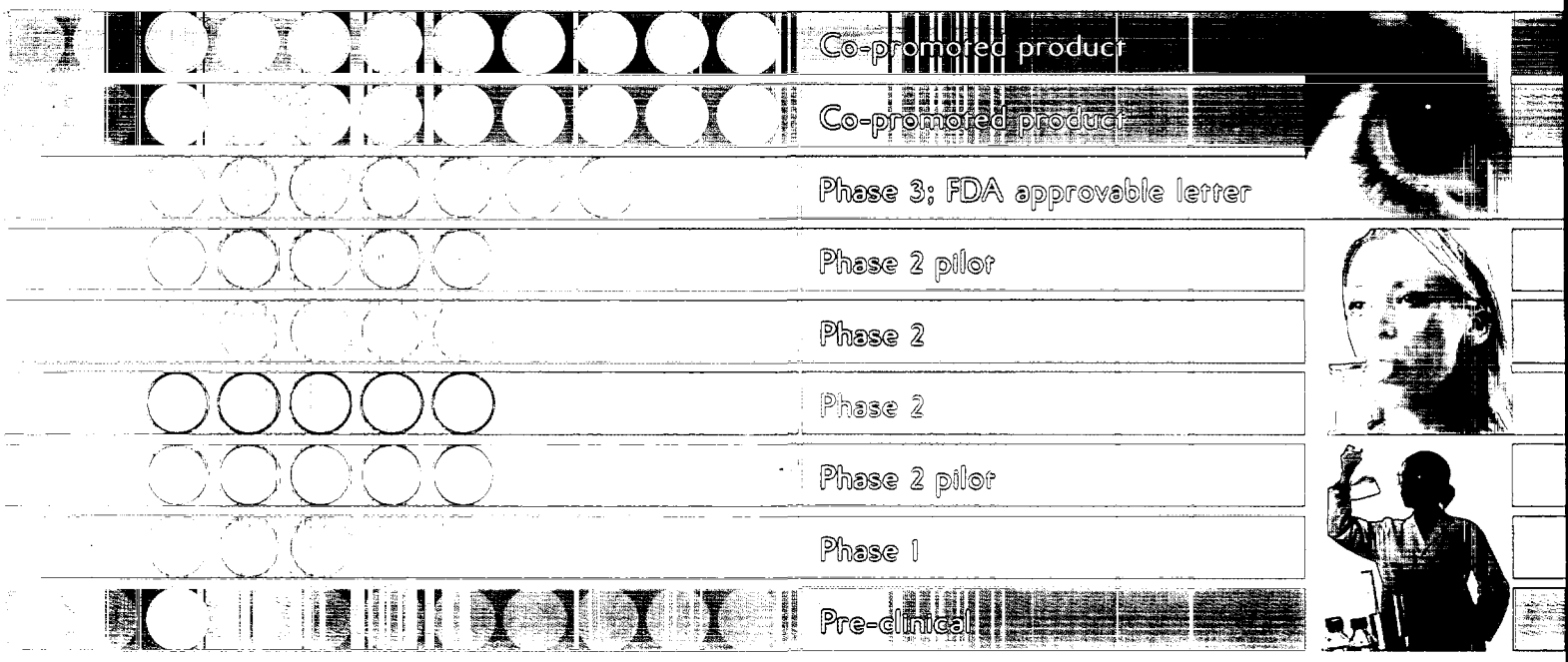
SEEING NEW SOLUTIONS

INSPIRE'S PORTFOLIO

ELESTAT™	allergic conjunctivitis
RESTASIS®	dry eye disease
DIQUAFOSOL TETRASODIUM	dry eye disease
DIQUAFOSOL TETRASODIUM	corneal wound healing
INS37217 RESPIRATORY (denufosol tetrasodium)	cystic fibrosis
INS37217 OPHTHALMIC (denufosol tetrasodium)	retinal detachment
INS37217 OPHTHALMIC (denufosol tetrasodium)	macular edema
INS50589 ANTIPLATELET	cardiovascular diseases
DISCOVERY PROJECT	glaucoma

FIVE KEYS TO INSPIRE'S BUSINESS STRATEGY

1. Patient Focus—new approaches to treating disease and addressing patient needs
2. Breakthrough Science—aggressive pursuit of novel technologies
3. Expanding Pipeline—experienced development team advancing the pipeline
4. Effective Commercial Team—focused commercial capability
5. Strategic Partnering—proactive approach to licensing and collaborations



TO OUR STOCKHOLDERS:

"We have a committed and experienced team that continues to work diligently toward our goal of building a strong, sustainable business that delivers benefit to patients and value to stockholders."

Christy L. Shaffer, Ph.D.

2004 was an important year in Inspire's history as we transformed from a development stage company to a commercial organization with a focused marketing and sales team that complements our research and development capabilities. These combined capabilities differentiate Inspire from many other biotechnology and specialty pharmaceutical companies. We are proud of the many accomplishments that our team achieved during the year.

2004 Accomplishments

- Launched and initiated U.S. co-promotion of Elestat™, an allergic conjunctivitis product
- Initiated U.S. co-promotion of Restasis®, a dry eye product, with Allergan, Inc.
- Generated co-promotion revenue of $11.1 million
- Launched and completed enrollment in an additional Phase 3 dry eye clinical trial of diquafosol
- Completed and reported results of a Phase 2 cystic fibrosis clinical trial and initiated long-term toxicology studies of INS37217 Respiratory
- Filed an Investigational New Drug (IND) application with the Food & Drug Administration (FDA) for INS50589 Antiplatelet for cardiovascular indications and initiated a Phase 1 clinical trial
- In-licensed patents related to a novel approach for treating glaucoma
- Raised approximately $120 million in equity capital to fund growth
- Created a business development function to proactively pursue strategic partnership opportunities

Our New Commercial Team: A Strong Start

We completed the hiring of our marketing and sales team in January of 2004, began co-promotion of Restasis for dry eye disease and launched Elestat for allergic conjunctivitis. Both of these products were developed by our partner, Allergan, Inc. Our territory managers and regional directors rapidly established strong relationships with the top 200 highest prescribing ophthalmologists, optometrists and allergists in each of our 64 territories, and through a dedicated and professional effort drove Elestat to become the second most prescribed allergic conjunctivitis product among this group of targeted specialists, according to data from IMS Health.

Dry Eye: A Challenging Pathway for an Important Potential Product

In 2004, we successfully enrolled more than 600 patients in a Phase 3 clinical trial of diquafosol tetrasodium in patients with dry eye disease. This clinical trial was initiated following the FDA's review of our New Drug Application (NDA) and subsequent approvable letter. While we did not achieve the primary endpoint in this clinical trial, we did achieve a number of secondary endpoints. We have decided to submit an amendment to our NDA and to seek FDA approval of diquafosol based on the totality of data we have accumulated on the safety and efficacy of diquafosol for dry eye from our various clinical trials. We recognize that obtaining FDA approval without having achieved primary endpoints in multiple key studies is likely to be an uphill battle; however, we believe that

Pictured in left photo: One of Inspire's founding scientists and a world-renowned clinician in cystic fibrosis works with one of his patients, who is an Inspire employee.

PATIENT FOCUS

"We know that what we do each day makes a difference"

from Inspire's "Who We Are" corporate statement

Inspire is a biopharmaceutical company dedicated to discovering, developing and commercializing prescription pharmaceutical products in disease areas with significant commercial potential and unmet medical needs. This includes targeting therapeutic markets and pursuing product candidates where current therapy is not optimal. Our focus is on improving outcomes and the quality of life for the patient.

With a talented team of more than 165 employees, Inspire is dedicated to building and commercializing a sustainable pipeline of innovative new treatments based upon technical and scientific expertise, focusing in the ophthalmic and respiratory therapeutic areas. We have a strong focus in the therapeutic area of ophthalmology with programs targeted toward addressing needs in allergic conjunctivitis, dry eye disease, corneal wound healing, retinal disease and glaucoma. We are also working on a product candidate for the treatment of respiratory complications of cystic fibrosis and an antiplatelet product candidate that could be utilized in cardiopulmonary bypass procedures.

delivering to the FDA a complete package of data on the safety and efficacy of this potential product is a worthwhile effort and is the most appropriate next step in this challenging process. We expect to submit the NDA amendment by the end of the second quarter of 2005. We continue to believe that diquafosol provides benefit to patients with dry eye and we are pleased that the medical community remains enthusiastic regarding potential new pharmaceutical products for this area of high unmet medical need.

Pipeline: Progressing Our Opportunities

We enhanced our pipeline in 2004 through in-licensing and by advancing our most promising programs. Most notably, we reported positive Phase 2 clinical trial results in our cystic fibrosis program, INS37217 Respiratory, and initiated long-term toxicology studies that are required before advancing to Phase 3. In 2005, we expect to complete the toxicology studies as well as an additional Phase 2 clinical trial that will aid us in the design of our Phase 3 program. We plan to request a meeting with the FDA when we have results from the additional Phase 2 clinical trial and toxicology studies, and we expect to finalize plans for our Phase 3 program for INS37217 Respiratory by the end of 2005. We intend to maintain marketing and sales responsibility for INS37217 Respiratory in North America and to identify a partner for commercializing this cystic fibrosis product candidate outside of North America.

We progressed a key discovery program in 2004 by filing an IND application and launching a Phase 1 clinical trial for INS50589 Antiplatelet. This potential product is attractive in that it has a rapid onset and offset of action, unlike currently marketed antiplatelet products. We expect to report results from this Phase 1 clinical trial by the middle of 2005. Given our current therapeutic focus and the significant level of resources necessary to develop a cardiovascular product, we plan to identify potential partnership opportunities for this program.

We intensified our focus on ophthalmology over the past year and further strengthened our pipeline in this area through in-licensing and by identifying potential new indications for current programs. In 2004, we in-licensed patents from the national award-winning technology transfer organization, Wisconsin Alumni Research Foundation, and we are excited about the potential to provide a new approach to the treatment of glaucoma. In addition, in early 2005, we began designing Phase 2 pilot studies of INS37217 Ophthalmic in macular edema associated with uveitis and post-cataract surgery and a Phase 2 pilot study of diquafosol in corneal wound healing. We expect to conduct and report results of these pilot studies by the end of 2005.

The Inspire Team: Experienced and Committed

Our ability to successfully advance our research and development programs is based largely on the strength of our employees. One of our key achievements in 2004 was the recruitment of key staff in multiple areas of the business including Ophthalmology R&D, Marketing and Sales, Business Development and Legal. We pride ourselves in having a dynamic and supportive

W. LEIGH THOMPSON, M.D., PH.D., SCD

1938–2005

Dr. Leigh Thompson will be remembered for his tremendous contributions to Inspire and the broader scientific and medical community. His pioneering efforts in critical care, pharmaceutical development innovations, and information technology management have made a lasting positive impact on the medical community.

Dr. Thompson began his service as a director of Inspire in 1996 and served as Chairman of the Board beginning in 2002. In 1994, Dr. Thompson retired from Eli Lilly and Co. where he served as Chief Scientific Officer and a member of the management committee. Dr. Thompson enjoyed a distinguished career in both academic medicine and the pharmaceutical industry. He published extensively, particularly in the area of critical care medicine. One of the highlights of his career was the discovery of the lifesaving blood substitute, hetastarch. Dr. Thompson was a member of numerous corporate, academic, and civic boards, and consulted in the areas of health informatics, enterprise strategic planning, and related areas. In 2003, he was inducted into the Johns Hopkins Society of Scholars.

Also in 2003, the FDA awarded Dr. Thompson the Commissioner's Special Citation for Multiple Innovative Contributions to Public Health and Wellbeing. According to the FDA, in a career spanning nearly four decades, Dr. Thompson made significant contributions to medical care, drug development and the public health.

His guidance will be missed.

corporate culture that allows us to attract and retain great people. In the past two years, we have been publicly recognized as a highly desirable place to work and for our contributions to the community. We believe that retaining our exceptional employees will continue to be a key factor in our ability to succeed and thrive.

Another important part of the Inspire team is our talented and experienced Board of Directors. In February 2005, we were saddened by the loss of our Chairman of the Board, W. Leigh Thompson, M.D., Ph.D., ScD. We will miss his wisdom and steadfast support. We have dedicated a special foldout section on this page in remembrance of his tremendous contributions. Our Board made a smooth transition by naming a new Chairman, Kenneth B. Lee, Jr., who had previously served as the Board's Vice Chairman. We appreciate the service, dedication and valuable advice provided by all of our Board members.

The Future: Progress and Prudence

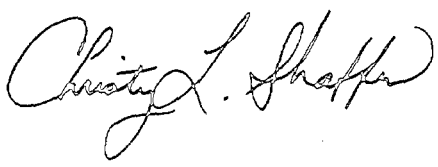
We intend to judiciously allocate our resources to the maximum potential, advancing our most promising product candidates, attempting to out-license programs where appropriate and furthering our commercial initiatives with intense focus on key value drivers.

In 2005, we intend to focus on three major goals:

- To build a comprehensive data package to submit a NDA amendment to the FDA on diquafosol for the treatment of dry eye disease;
- To prudently shepherd our cash. We have a strong balance sheet with more than two years of cash, based on current internal projections, and we intend to allocate this capital to key value drivers; and
- To aggressively advance our high priority programs and key business development efforts.

We are in a strong position to continue investing in our pipeline and our commercial efforts. We are pleased with the growth of both Elestat and Restasis and together with our partner, Allergan, we intend to continue to drive sales of these products in 2005, while pursuing additional partnering opportunities to further enhance the value that our commercial team brings to Inspire.

The road ahead of us is both exciting and challenging. We have a committed and experienced team that continues to work diligently toward our goal of building a strong, sustainable business that delivers benefit to patients and value to stockholders. We intend to capitalize on our core strategies–patient focus, breakthrough science, expanding pipeline, effective commercial team and strategic partnering–to grow our business and achieve success in 2005 and beyond.



Christy L. Shaffer, Ph.D.
Chief Executive Officer

BREAKTHROUGH SCIENCE

Inspire's experienced scientists apply their expertise to fuel the product pipeline through novel in-house research combined with strategic in-licensing opportunities.

At Inspire, we have assembled a highly experienced team of scientists with substantial expertise in drug discovery and development. This team drives the expansion of our pipeline of product compounds through our own research activities, strategic in-licensing of novel technologies and further in-house development and expansion of these technologies.

Our original technology, focusing on the $P2Y_2$ receptor, was licensed from the University of North Carolina at Chapel Hill (UNC) in the mid 1990s. Inspire scientists, working with UNC researchers, immersed themselves in this emerging field, and were soon recognized as leaders in the discovery and synthesis of nucleotides that activate the $P2Y_2$ receptor. Our significant expertise and proprietary knowledge relating to the design and synthesis of P2 receptor agonists and antagonists has led to patentable discoveries for the treatment of ophthalmic, respiratory and cardiovascular diseases.

This strategy of combining strategic in-licensing with focused in-house technology development has also fueled our antiplatelet and glaucoma programs. The antiplatelet program was developed from another collaboration with UNC in 2002. The $P2Y_{12}$ technology initially licensed has since been expanded by Inspire scientists who have synthesized an intravenous compound that is now in Phase 1 development and identified a novel chemical lead series of $P2Y_{12}$ receptor antagonists with oral bio-availability.

In 2004, we continued to employ this strategy by in-licensing patents from the Wisconsin Alumni Research Foundation relating to a potential new mechanism of action for reducing intraocular pressure to treat glaucoma. Our scientists are now engaged in the identification and synthesis of compounds that target the trabecular meshwork to improve aqueous humor outflow and may provide a new approach to the reduction of intraocular pressure in glaucoma patients.

Pictured in photo above: Senior Vice President, Discovery, Ben Yerxa (left); Senior Vice President, Ophthalmic Research and Development, Kim Brazzell (right).

3 EXPANDING PIPELINE

Our goal at Inspire is to build and commercialize a sustainable pipeline of innovative new treatments based on technical and scientific expertise, focusing in the ophthalmic and respiratory therapeutic areas. Our development strategy is to advance multiple product candidates in areas where Inspire has significant expertise, through targeted drug discovery, efficient clinical development, strategic alliances and in-licensing.

Since Inspire's inception, we have expanded our intellectual property position to nearly 50 patents. Many of these patents reflect the expansion of licensed technology to new therapeutic indications or new classes of compounds. The concept of using $P2Y_2$ receptor agonists to treat fluid transport associated with respiratory disease was expanded to target potential new products for ophthalmic disorders in which fluid transport plays a key role, such as dry eye and retinal disease. In addition, recent research on the role of $P2Y_2$ receptors in the epithelial healing process has led us to evaluate the benefit of $P2Y_2$ agonists in corneal wound healing.

Inspire works closely with clinical investigators and regulatory authorities to navigate the lengthy and rigorous pharmaceutical development process.

Our scientists actively pursue and explore potential expansions of existing technologies and programs. Since 1997, Inspire has filed seven IND applications with the FDA for product candidates that were subsequently evaluated in humans. Several of these product candidates have progressed to later phases of development. This proven ability to expand our potential product opportunities by capitalizing on novel discoveries is one key element in our strategy to build and maintain a sustainable pipeline.

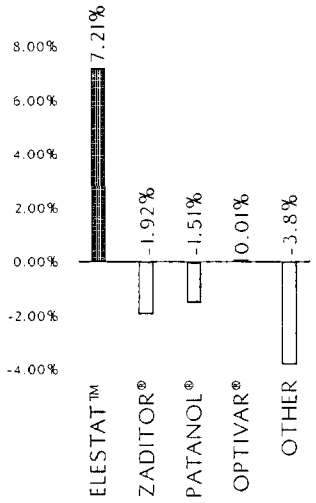
Complementing our in-house efforts toward expanding our existing pipeline, our recently established business development function is working to provide new product opportunities across all phases of our business—discovery, development and commercial.

Pictured in photo below: Senior Vice President, Development, Don Kellerman (left); Vice President, Pharmaceutical Development, Richard Evans (right).

Pictured in inset photo: Senior Vice President, Marketing and Sales, Joe Schachle.

EFFECTIVE COMMERCIAL TEAM

IMPACT OF INTRODUCTION OF ELESTAT™ IN ALLERGIC CONJUNCTIVITIS MARKET
2004 Change in Total Prescription Market Share Since Launch of Elestat™



Source: IMS National Prescription Audit Weekly Data (Jan.–Dec. 2004)

A key element of Inspire's strategy is to successfully commercialize products through a concentrated marketing and sales effort in target U.S. markets. In 2004, we completed the hiring and training of an experienced sales force of 64 territory managers, plus a focused sales management, marketing and training staff. This bright, hardworking and highly motivated marketing and sales organization successfully launched Elestat™, a topical treatment for ocular itching associated with allergic conjunctivitis, and began co-promotion activities for Restasis®, a topical cyclosporine treatment for inflammatory-based dry eye.

The impact of our salesforce on generating patient and physician acceptance of both products has been very positive. Elestat continues to increase market share and to be widely accepted by patients and physicians, becoming the second most prescribed allergic conjunctivitis product among the 12,800 highest-prescribing ophthalmologists, optometrists, and allergists in the United States, according to data from IMS Health. In addition, sales of Restasis have been growing at an attractive rate, with the product responding well to Allergan's direct to consumer advertising campaign and Allergan and Inspire's promotion efforts.

There are several potential benefits to having integrated marketing and sales capabilities, including generating revenues, maintaining greater control over commercialization of pipeline products, enhancing the ability to attract desirable partnerships and increasing potential royalty rates with partners. The commercialization activities have also been instrumental in building corporate awareness in the medical and scientific communities, since the packaging and marketing materials for the current co-promoted products carry both the Allergan and Inspire names and logos.

Pictured in inset photo (left to right): Executive Vice President, Corporate Development and General Counsel, Barry Pea; Executive Vice President, Operations and Communications, Mary Bennett; Chief Financial Officer and Treasurer, Tom Staab.

STRATEGIC PARTNERING

Inspire's cross-functional approach to partnering includes leveraging in-house scientific, financial, intellectual property and business development resources to identify, develop and secure strategic relationships.

Inspire is focused on establishing strategic relationships that enhance and complement our product development and commercial organization. Collaborations are a key component of our corporate strategy. We have a history of global strategic collaborations and partnerships, including relationships with Allergan, Inc., Santen Pharmaceutical Co., Ltd., Cystic Fibrosis Foundation Therapeutics, Inc., Wisconsin Alumni Research Foundation and UNC, among others. In addition, we utilize sponsored research agreements as an effective way to access academic experts in our areas of interest and fund research that could significantly enhance our understanding of and access to potential product opportunities. Importantly, Inspire was founded on technology licensed from UNC, based upon research conducted by UNC's well-respected physicians and researchers at the Cystic Fibrosis Pulmonary Treatment and Research Center.

From a strategic perspective, we will continue to pursue opportunities to (1) bring in new products, technologies or intellectual property and (2) out-license certain rights to proprietary technologies or pharmaceutical product candidates developed by Inspire that are outside our core therapeutic areas of focus. In 2004, we increased our commitment to business development activities through the hiring of several key staff and the creation of a formal function focused on pursuing strategic partnership opportunities. In 2005, we have several objectives in this area, including identifying potential partners for the marketing of our cystic fibrosis product candidate outside of North America and the development and commercialization of INS50589 Antiplatelet for cardiovascular indications.

INSPIRE

2004

FORM 10-K

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2004

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to .

Commission File No. 000-31135

INSPIRE PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	04-3209022
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
4222 Emperor Boulevard, Suite 200, Durham, North Carolina	**27703-8466**
(Address of Principal Executive Offices)	(Zip Code)

(919) 941-9777
(Registrant's telephone number, including area code)

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

Title of Each Class	Name of Each Exchange on Which Registered
None	None

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $.001 par value
(Title of Class)

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 an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes ☒ No ☐

State the aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter. $530,885,414.

Indicate the number of shares outstanding of each of the Registrant's classes of common stock, as of January 31, 2005.

Class	Number of Shares
Common Stock, $.001 par value	41,861,280

Documents incorporated by reference

Document Description	10-K Part III
Portions of the Registrant's proxy statement to be filed pursuant to Regulation 14A within 120 days after Registrant's fiscal year end of December 31, 2004 are incorporated by reference into Part III of this report.	Items 10, 11, 12, 13, 14

INSPIRE PHARMACEUTICALS, INC.
2004 FORM 10-K ANNUAL REPORT

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PART I

Item 1. Business.

Overview

We are a biopharmaceutical company dedicated to discovering, developing and commercializing prescription pharmaceutical products in disease areas with significant commercial markets and unmet medical needs. Our goal is to build and commercialize a sustainable pipeline of innovative new treatments based upon our technical and scientific expertise, focusing in the ophthalmic and respiratory therapeutic areas. Our ophthalmic products and clinical product candidates are currently concentrated in the allergic conjunctivitis, dry eye disease, corneal wound healing and retinal disease indications. In addition, we also have a preclinical program to treat glaucoma. We are also working on a product candidate for the treatment of respiratory complications of cystic fibrosis and an antiplatelet product candidate that could be utilized in cardiopulmonary bypass procedures. Our portfolio of products and product candidates include:

PRODUCTS AND PRODUCT CANDIDATES	THERAPEUTIC AREA/ INDICATION	COLLABORATIVE PARTNER	CURRENT STATUS
Products			
Elestat™	Allergic conjunctivitis	Allergan	Co-promoting in the United States since February 2004
Restasis®	Dry eye disease	Allergan	Co-promoting in the United States since January 2004
Product Candidates in Clinical Development			
diquafosol tetrasodium (INS365 Ophthalmic)	Dry eye disease	Allergan and Santen Pharmaceutical	FDA approvable letter received December 2003, NDA amendment filing expected by June 30, 2005
	Corneal wound healing	Allergan and Santen Pharmaceutical	Phase 2 pilot study to be initiated by March 2005
INS37217 Respiratory (denufosol tetrasodium)	Cystic fibrosis	Cystic Fibrosis Foundation Therapeutics	Phase 2
INS37217 Ophthalmic (denufosol tetrasodium)	Retinal detachment	None	Phase 2
	Macular edema	None	Phase 2 pilot studies to be initiated in 2005
INS50589 Antiplatelet	Cardiovascular diseases	None	Phase 1

We have acquired the rights to market Elestat™ and Restasis® in the United States under co-promotion agreements with Allergan, Inc., or Allergan, and we receive co-promotion revenue based upon net sales of these products. In January 2004, we completed the hiring and training of our specialty sales force, at which time we began co-promoting Restasis® for dry eye disease. In February 2004, we launched Elestat™ for the treatment of allergic conjunctivitis.

We have several product candidates in various stages of clinical development and various programs in preclinical development. All of our clinical product candidates are based on proprietary technology relating to P2 receptors. Our most clinically advanced product candidates are $P2Y_2$ receptor agonists that target ophthalmology and respiratory conditions and diseases where current treatments are not adequate.

We were incorporated in October 1993 and commenced operations in March 1995 following our first substantial financing and licensing of the initial technology from The University of North Carolina at Chapel Hill, or UNC. We are located in Durham, North Carolina, adjacent to the Research Triangle Park.

Our Strategy

Our business objective is to become a leading biopharmaceutical company focused on discovering, developing and commercializing new treatments for diseases primarily in the ophthalmic and respiratory areas. We intend to build and commercialize a sustainable pipeline of innovative new treatments based on our technical and scientific expertise, focusing in the ophthalmic and respiratory therapeutic areas. Our strategy is to advance multiple product candidates in areas where we have significant expertise, through drug discovery, clinical trials, strategic alliances and in-licensing, and to be involved in the marketing and sale of our products. The principle elements of our strategy are to:

- **Aggressively Advance Our Product Candidates.** We focus significant energy and resources to rapidly and efficiently develop our existing product candidates. We target therapeutic markets and pursue product candidates where current therapy is not optimal and where we perceive significant market opportunities to exist.
- **Establish Strategic Relationships that Enhance and Complement Our Own Product Development and Commercial Organization.** Collaborations are, and we believe will continue to be, a key component of our corporate strategy. We have entered into alliances with pharmaceutical companies for the commercialization of our products, especially to address markets outside North America where we do not intend to develop infrastructure to commercialize our products. In addition, we intend to continue to develop alliances with leading pharmaceutical companies to enrich our product candidate pipeline and optimize our commercial efforts.
- **Successfully Commercialize Products Through a Concentrated Sales and Marketing Effort in Our Target Markets.** A key element of our strategy is to be involved in the sales and marketing activities of our products in North America. To that end, we have developed a specialty sales and marketing organization to support the commercialization of Elestat™ and Restasis® to ophthalmologists, optometrists and allergists in the United States.
- **Develop or In-License New Products Outside Our Original Proprietary P2 Technology Platform.** Our research focus is to discover new pharmaceutical products that expand upon and beyond our P2 receptor technology. We have internal programs and sponsored research and development agreements with universities to discover, develop and in-license new pharmaceutical products. We intend to be opportunistic with regard to in-licensing products in various stages of development in our core therapeutic areas.
- **Protect and Enhance Our Technology Leadership Position.** We have a substantial intellectual property position related to our technology. We currently have 48 issued patents: 26 exclusively owned, 7 jointly owned and exclusively licensed, 12 exclusively licensed, and 3 non-exclusively licensed. We also have other U.S. patents pending and multiple foreign patents issued and pending. We intend to continue to pursue an aggressive patent strategy to protect our expanding proprietary discoveries.

Elestat™

Overview. In December 2003, we entered into an agreement with Allergan to co-promote Elestat™ (epinastine HCl ophthalmic solution 0.05%) to ophthalmologists, optometrists and allergists in the United States.

Under this agreement, we receive co-promotion revenue from Allergan on the U.S. net sales of Elestat™. The Elestat™ arrangement with Allergan will be in effect until the earlier of: (i) the approval and launch of the first generic epinastine product; or (ii) the approval and launch of the first over-the-counter epinastine product. The commercial exclusivity period for Elestat™ under the Hatch-Waxman Act will expire in October 2008, after which time Elestat™ could face generic competition. The agreement also provides for early termination under certain circumstances.

Elestat™ was approved by the U.S. Food and Drug Administration, or FDA, in October 2003 for the prevention of itching associated with allergic conjunctivitis. In February 2004, we launched Elestat™ in the United States and are promoting it to eye care professionals and allergists. Elestat™, a topical antihistamine with mast cell stabilizing and anti-inflammatory activity, was developed by Allergan for the relief of ocular itching associated with ocular allergies. Elestat™ works by blocking the H_1 and H_2 histamine receptors, stabilizing mast cells, and stopping the progression of pro-inflammatory mediators.

Market Opportunity. Allergies affect more than 40 million people in the United States annually, including 20% to 30% of adults and up to 40% of children. It has been estimated that allergic conjunctivitis may occur in up to 90% of those patients suffering from allergies. The annual United States market for prescription ocular allergy products is approximately $390 million. The prescription market has experienced a growth rate, in terms of dollars, of approximately 12% over 2003. Elestat™ is indicated for adults and children at least 3 years old.

Co-Promotion Agreement. We have the primary responsibility for selling, promotional and marketing activities of Elestat™ in the United States and are responsible for the associated costs. We work with Allergan collaboratively on overall product strategy and management in the United States. Allergan records sales of Elestat™ and remains responsible for all other product costs. Allergan retains the licensing rights relating to promotion of Elestat™ to U.S. prescribers other than ophthalmologists, optometrists and allergists; but we have a right of first refusal to obtain such rights in the event Allergan decides to engage a third party to undertake such activities. Under the terms of the agreement, we paid Allergan an up-front payment and Allergan pays co-promotion revenue to us on U.S. net sales of Elestat™, except in the event that a third party is engaged by Allergan to promote Elestat™ to prescribers outside of our field, in which case we will be paid a proportionate share of U.S. net sales of Elestat™ based upon filled prescriptions written by ophthalmologists, optometrists and allergists. Allergan also retains rights to all international sales and marketing activities relating to the drug. See "—Collaborative Agreements."

Restasis®

Overview. In June 2001, we entered into a joint license, development and marketing agreement with Allergan to develop and commercialize diquafosol tetrasodium (INS365 Ophthalmic) for the treatment of dry eye disease. The agreement also granted us the right to co-promote Allergan's Restasis® (cyclosporine ophthalmic emulsion) 0.05% for the treatment of dry eye disease in the United States. In December 2002, Restasis® was approved for sale by the FDA and Allergan launched Restasis® in the United States in April 2003. In the third quarter of 2003, we exercised our right to co-promote Restasis® under the joint license, development and marketing agreement with Allergan. In January 2004, we began co-promotion of Restasis® to eye care professionals and allergists in the United States and began receiving co-promotion revenue on net sales of Restasis® beginning in April 2004. Restasis® is the first approved prescription product in the United States for dry eye disease. It is indicated to increase tear production in patients with keratoconjunctivitis sicca, or dry eye disease, whose tear production is presumed to be suppressed due to ocular inflammation.

Market Opportunity. Other than Restasis®, the current treatments for dry eye disease in the major markets consist of artificial tear solutions and lubricant eye drops. In some cases, small plugs are inserted by physicians in the tear duct to slow tear drainage. Artificial tears, which are available as over-the-counter and, in some countries, as prescription products, provide temporary relief of symptoms, but can also wash out the natural proteins and other components that keep an eye healthy. We estimate, based on an extrapolation from U.S. data,

that dry eye disease affects approximately thirty million people in the eight major international prescription pharmaceutical markets, of which nine million are in North America. Dry eye disease can be caused by various factors including eye stress, aging, environmental factors, autoimmune disorders and various medications. Since dry eye disease is more prevalent among the elderly and post-menopausal women, this market is expected to grow as populations age. Based upon IMS and Verispan data sources, Allergan estimates the world-wide artificial tear and therapeutic dry eye market to be approximately $790 million and growing at a 20% rate based upon a moving twelve-month average as of September 2004. In the summer of 2005, Allergan commenced a direct-to-customer (DTC) advertising campaign of Restasis® which we believe had a positive impact on sales of Restasis®. For the year ending December 31, 2004, Allergan has recognized approximately $100 million of revenue from sales of Restasis®. Allergan forecasts 2005 sales of Restasis® to be between $140-160 million.

Collaborative Agreement. In December 2003, at the time we entered into the co-promotion agreement relating to Elestat™, we amended the joint license, development and marketing agreement to reduce the co-promotion revenue rates that we would receive upon the sale of Restasis®. See "—Collaborative Agreements."

Diquafosol tetrasodium (INS365 Ophthalmic)

Treatment of dry eye disease

Overview. Diquafosol is an ophthalmic product candidate designed to treat dry eye disease and is expected to be used alone or as a complement to Restasis®, if and when it receives regulatory approval. Diquafosol is a dinucleotide that we discovered, which functions as an agonist at the $P2Y_2$ receptor. Diquafosol stimulates the release of natural tear components targeting all three mechanisms of action involved in tear secretion – mucin, lipids and fluid. To date, we have completed four Phase 3 clinical trials of diquafosol for the treatment of dry eye disease. In total, we have conducted placebo-controlled clinical trials of diquafosol in more than 2,000 individuals.

We are developing diquafosol as an eye drop for dry eye disease. We believe that diquafosol could be the second FDA approved pharmacologically active agent to treat dry eye disease, and the first one with this mechanism of action. Because diquafosol and Restasis® have different mechanisms of action, we consider them complementary products and believe there is commercial opportunity for these products.

Development Status. On June 27, 2003, we filed a New Drug Application, or NDA, with the FDA for diquafosol for the treatment of dry eye disease. In July 2003, the FDA granted Priority Review designation for the diquafosol NDA. On December 19, 2003, we received an approvable letter from the FDA for diquafosol for the treatment of dry eye disease. Since the initial submission of the NDA, we have completed two additional diquafosol Phase 3 clinical trials, trials 108 and 109. Although neither of the two additional diquafosol Phase 3 clinical trials met their primary endpoint, we plan to submit an amendment to our diquafosol NDA by June 30, 2005 based upon the totality of data from our diquafosol clinical program, including positive data on certain secondary endpoints and analyses from the 108 and 109 clinical trials.

Pursuant to our agreement with Allergan, Allergan is responsible for regulatory approval of diquafosol in Europe. We intend to consult with Allergan to determine a European regulatory filing strategy for diquafosol for the treatment of dry eye disease.

Estimated subsequent costs necessary to amend our diquafosol NDA submission and resubmit the application for commercial approval in the United States are projected to be in the range of $0.5 to $1.5 million, excluding the cost of pre-launch clinical product inventory. This estimate includes costs for completing the Phase 3 diquafosol 109 clinical trial, salaries for development personnel, regulatory and consulting costs associated with our NDA amendment and other unallocated development costs. Costs of any other diquafosol clinical trials and any costs associated with a potential corneal wound healing indication for diquafosol are excluded from this

projection. The projected costs associated with such estimate are difficult to determine and the actual costs are likely to differ. For a more detailed discussion of the risks associated with the development of diquafosol and our other development programs, including factors that could result in a delay of a program and increased costs associated with such a delay, please see the Risk Factors described elsewhere in this report.

Collaborative Agreements. Under the joint license, development and marketing agreement with Allergan, we have continued our efforts to develop and commercialize diquafosol. Under this agreement, we have received up-front and milestone payments of $11 million and may receive up to an additional $28 million in milestone payments assuming the successful completion of all remaining milestones under this agreement. We will also receive co-promotion revenue from Allergan on net sales, if any, of diquafosol worldwide, excluding most larger Asian markets. In the third quarter of 2003, we exercised our right under the Allergan agreement to co-promote diquafosol with Allergan in the United States and expect to begin promoting this product if and when we receive FDA approval and the product is launched. Our partner, Santen Pharmaceutical Co., Ltd., or Santen, is developing diquafosol in Japan and nine other Asian countries. Diquafosol is currently in Phase 2 clinical trials in Japan. See "—Collaborative Agreements."

Treatment of corneal wound healing

We are also evaluating diquafosol in a corneal epithelial wound healing indication. There is support for the wound healing potential of diquafosol based on both preclinical and clinical experience. We are planning to initiate a Phase 2 pilot study of diquafosol in subjects undergoing Photorefractive Keratectomy surgery in March 2005. This study will evaluate the healing rate of the cornea comparing diquafosol versus placebo. Our collaborative agreements with Allergan and Santen cover this potential indication, as well as dry eye disease. See "—Collaborative Agreements."

INS37217 Respiratory (denufosol tetrasodium) for the treatment of cystic fibrosis.

Overview. We are developing INS37217 Respiratory (denufosol tetrasodium) as an inhaled product candidate for the treatment of cystic fibrosis. We believe that our product candidate could be the first FDA approved product that mitigates the underlying ion transport defect in the airways of patients with cystic fibrosis. This product candidate has been granted orphan drug status by the FDA and fast-track review status. INS37217 Respiratory is designed to enhance the lung's innate mucosal hydration and mucociliary clearance mechanisms which in cystic fibrosis patients are impaired due to a genetic defect. By hydrating airways and stimulating mucociliary clearance through stimulation of the $P2Y_2$ receptor, we expect to help keep the lungs of cystic fibrosis patients clear of thickened mucus, reduce infections and limit the damage that occurs as a consequence of the prolonged retention of thick and tacky infected secretions. Based upon the results of recent clinical data, we believe this product candidate could be complementary to Pulmozyme®.

Cystic fibrosis is a life-threatening disease involving a genetic mutation that disrupts the cystic fibrosis transmembrane regulator protein, an ion channel. In cystic fibrosis patients, a defect in this ion channel leads to poorly hydrated lungs and severely impaired mucociliary clearance. Chronic secondary infections invariably occur, resulting in progressive lung dysfunction and deterioration. Respiratory infections and complications account for more than 95% of the morbidity and mortality associated with this disease. According to the United States Cystic Fibrosis Foundation, the median life expectancy for patients is 33 years.

Development Status. In 2003, we initiated a multi-center Phase 2 clinical trial in 90 patients with mild cystic fibrosis lung disease that was conducted in collaboration with the Cystic Fibrosis Foundation Therapeutics, Inc., or the CFFT. In October 2004, we presented detailed results of this clinical trial at the North American Cystic Fibrosis Conference. This clinical trial was a double-blind, placebo-controlled, randomized trial over a four-week treatment period. The primary purpose of this clinical trial was to determine tolerability of three times daily nebulizer doses of up to 60 mgs of INS37217 Respiratory versus placebo over a four-week treatment period. Patients receiving INS37217 Respiratory (pooled results across three doses) had significantly better lung function

than patients receiving placebo after 28 days of treatment. Lung function was assessed by multiple standard spirometric measurements and statistical significance was achieved on all of the spirometric measures employed in the clinical trial. All three doses were well tolerated over the four-week treatment period.

Following discussions with the FDA in September 2004, we have begun long-term toxicology studies in two animal species. We have also initiated an additional Phase 2 clinical trial in approximately 70 patients with cystic fibrosis lung disease in parallel with these toxicology studies in order to broaden our patient experience prior to our initiation of a Phase 3 program. The primary purpose of this additional Phase 2 clinical trial is to assess the safety and tolerability of INS37217 Respiratory in patients with more impaired lung function and taking more concomitant medications, such as inhaled antibiotics, than patients studied in our previous Phase 2 clinical trial. This ongoing Phase 2 clinical trial is not intended to show significant treatment effects, but rather to determine whether patients with lower lung function and those taking other concomitant cystic fibrosis medications, such as inhaled tobramycin, or TOBI®, could be included in our anticipated Phase 3 program for INS37217 Respiratory. We anticipate holding an End of Phase 2 meeting with the FDA before the end of 2005.

Estimated subsequent costs necessary to submit an NDA for INS37217 Respiratory for the treatment of cystic fibrosis are projected to be in the range of $30 million to $50 million, excluding the cost of pre-launch clinical product inventory and any potential development milestones payable to the CFFT. This estimate includes completing the remaining components of our Phase 2 program, conducting a Phase 3 clinical program, manufacturing INS37217 for clinical trials and toxicology studies, producing qualification lots consistent with current Good Manufacturing Practice, or cGMP, standards, salaries for development personnel, other unallocated development costs and regulatory preparation and filing costs. These costs are difficult to estimate and actual costs could be materially different from our estimate. For example, clinical trials and toxicology studies may not proceed as planned, results from future clinical trials may change our planned development program, other parties may assist in the funding of our development costs, and our NDA filing could be delayed. For a more detailed discussion of the risks associated with our development programs, please see the Risk Factors described elsewhere in this report.

Market Opportunity. The current therapeutic approaches to address cystic fibrosis mainly treat the symptoms and are aimed at reducing respiratory infections and breaking up thickened mucous secretions that cause airflow obstruction and harbor bacteria. For example, TOBI® is an inhaled antibiotic that treats the infection, and Pulmozyme® is an inhaled protein that breaks up excessive DNA in cystic fibrosis mucus that reduces the thickness and tackiness of the respiratory secretions. While both products are approved for the treatment of cystic fibrosis, neither product is designed to address the underlying ion-transport defect, which results in dehydrated mucus and severely impaired mucociliary clearance.

There are approximately 30,000 diagnosed cystic fibrosis patients in the United States and we estimate approximately 75,000 in the eight major international prescription pharmaceutical markets. The average annual cost of medicine to treat a cystic fibrosis patient in the United States exceeds $35,000, and the annual healthcare cost for patients in the United States is over $1 billion. We estimate that in the United States sales of prescription pharmaceutical products to treat cystic fibrosis currently are in excess of $390 million annually.

We intend to retain the development and commercial rights for INS37217 Respiratory in North America but to seek a corporate partner to develop and commercialize the product outside of North America.

Collaborative Agreement. In October 2002, we entered into a study funding agreement with the CFFT pursuant to which they funded the majority of the external costs of one Phase 2 clinical trial for the treatment of cystic fibrosis in exchange for certain milestone payments. These milestone payments are contingent upon FDA approval, potential commercialization and achievement of certain aggregate sales volume in the first five years following product approval. In the event of FDA approval, we are obligated to pay to the CFFT, over a period of five years, an amount equal to a multiple of the clinical trial costs incurred by the CFFT as a development milestone payment, which is currently estimated to be approximately $12 million. Additionally, in the event

aggregate sales of the product exceed a certain level in the first five years subsequent to regulatory approval, we are obligated to pay the CFFT an additional $4 million sales milestone, payable over two years. See "—Collaborative Agreements."

INS37217 Ophthalmic (denufosol tetrasodium)

Treatment of retinal detachment

Overview. INS37217 Ophthalmic (denufosol tetrasodium) is an investigative new drug under evaluation for the treatment of retinal diseases associated with pathological sub-retinal or intra-retinal accumulation of fluid. We are developing INS37217 Ophthalmic as an intravitreal injection. INS37217 Ophthalmic has been shown in experimental models of retinal detachment to stimulate retinal re-attachment by increasing the reabsorption (i.e., draining) of extraneous sub-retinal fluid across the retinal pigment epithelium, a layer of cells involved in controlling proper hydration of the retina and sub-retinal space. INS37217 Ophthalmic may also be useful to treat other sight-threatening retinal diseases also associated with pathological accumulation of sub-retinal or intra-retinal fluid, including diabetic and non-diabetic macular edema. (see "Treatment of Macular Edema" below)

Development Status. In January 2004, we met with the FDA and were given guidance on the planning of a well-controlled Phase 2 clinical trial in INS37217 Ophthalmic for the treatment of retinal detachment. In April 2004, we began a 160-patient Phase 2 clinical trial of INS37217 Ophthalmic for the treatment of retinal detachment. The clinical trial provides for a single intravitreal injection or placebo and allows for up to two additional consecutive daily injections in patients who show signs of improvement following the previous injection. Enrollment in this clinical trial has progressed at a significantly slower rate than originally anticipated. We are unlikely to continue this clinical trial as designed due to the clinical trial's slow enrollment and are evaluating the viability of future development of INS37217 Ophthalmic for the treatment of retinal detachment.

If the INS37217 Ophthalmic program for the treatment of retinal detachment were to continue as currently designed, estimated subsequent costs necessary to submit an NDA for INS37217 Ophthalmic are projected to be in the range of $25 million to $35 million, excluding the cost of pre-launch clinical product inventory and development costs for other retinal diseases. This estimate includes any remaining Phase 2 clinical trials, a Phase 3 clinical program, manufacturing INS37217 for clinical trials and toxicology studies, producing qualification lots consistent with cGMP standards, salaries for development personnel, other unallocated development costs and regulatory preparation and filing costs. The range excludes costs associated with INS37217 Ophthalmic development for a macular edema indication for which Phase 2 pilot studies are expected to be conducted in 2005. These costs are difficult to estimate and actual costs could be materially different from our estimate. For example, clinical trials and toxicology studies may not proceed as planned, and results from future clinical trials may change our planned development program. For a more detailed discussion of the risks associated with our development programs, please see the Risk Factors described elsewhere in this report.

Market Opportunity. There are currently no pharmaceutical products approved for rhegmatogenous retinal detachment, or RRD. While surgical techniques used to reattach the retina have relatively high single-operation success rates of 60-95%, patients frequently suffer from post-surgical problems, including diminished visual acuity, loss of eye motility, misaligned eyes, protracted periods of convalescence, and post-operative pain and discomfort. By stimulating fluid reabsorption across the retinal pigment epithelium, INS37217 Ophthalmic may reverse the progression of RRD and stimulate retinal re-attachment in some RRD patients without the need for surgery. Approximately 50,000 retinal detachments occur each year in the United States.

Treatment of macular edema

Macular edema is a swelling of the central region of the retina (macula) that occurs as a result of disease, injury or ocular surgery. Macular edema is often responsible for central visual loss of variable severity. We expect to initiate two Phase 2 pilot studies in 2005; one in macular edema associated with uveitis (a complex intraocular inflammatory disease) and the other in macular edema occurring after cataract surgery.

INS50589 Antiplatelet

$P2Y_{12}$ receptor antagonist for the inhibition of platelet aggregation.

Overview. INS50589 Antiplatelet is a reversible $P2Y_{12}$ receptor antagonist that we are developing as an intravenous inhibitor of platelet aggregation for the use in the acute treatment of cardiovascular diseases. Platelets, small disc-shaped blood cells, are responsible for initiating and maintaining blood clots. Platelet activation occurs in response to pathological conditions such as the rupture of an atherosclerotic plaque or by the loss of the integrity of the endothelial cells lining the blood vessels. Platelet activation also occurs inappropriately during cardiovascular interventions such as cardiopulmonary bypass. Once activated, platelets are no longer able to participate in the clotting process after the surgery, resulting in postoperative blood loss due to platelet dysfunction. Inhibition of platelet $P2Y_{12}$ receptors by the treatment with INS50589 Antiplatelet may reduce the relative risk of bleeding complications and/or clotting events associated with acute cardiovascular interventions. INS50589 Antiplatelet will be administered intravenously and has a rapid onset and offset mechanism of action. In preclinical studies, it has been shown to produce dose-dependent and sustained inhibition of platelet aggregation during the administration of the drug and to protect against mortality resulting from systemic intravascular thromboembolism. We believe that the fast offset pharmacokinetic property, coupled with the ability to inhibit both platelet aggregation and degranulation/secretion, are key differentiating characteristics from other approved anti-platelet agents.

Development status. In November 2004, we filed an Investigational New Drug Application, or IND, and in December 2004, we initiated a Phase 1 clinical trial of the tolerability, pharmacokinetics and pharmacodynamics of INS50589 Antiplatelet in healthy volunteers. The clinical trial is a single-center, randomized, open labeled dose escalation, followed by a double-blind placebo-controlled clinical trial. We expect to complete the Phase 1 clinical trial and to finalize a key proof of concept animal study in this potential clinical indication in the first half of 2005. After reviewing the Phase 1 data, we intend to evaluate an appropriate partnering strategy for this product candidate. Given the limited data available and the early stage of development of this program, we are unable to reasonably project whether a Phase 2 or Phase 3 program would be appropriate for the product candidate and, if so, the future dates and costs that may be associated with such clinical trials or prospective NDA filing.

Additional discussion of the costs and expenses associated with all of our research and development programs is discussed below in "Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations—Years Ended December 31, 2004, 2003 and 2002—Costs and Expenses."

Collaborative Agreements

Allergan, Inc.—Elestat™

In December 2003, we entered into an agreement with Allergan to co-promote Elestat™ to ophthalmologists, optometrists and allergists in the United States. Elestat™ was approved by the FDA in October 2003 for the prevention of itching associated with allergic conjunctivitis. We have the primary responsibility for selling, promotional and marketing activities of Elestat™ in the United States and are responsible for the associated costs. We work with Allergan collaboratively on overall product strategy and management in the United States. Allergan records sales of Elestat™ and remains responsible for all other product costs, as well as retaining responsibility for all international marketing and selling activities. Allergan also retains the licensing rights relating to promotion of Elestat™ to U.S. prescribers other than ophthalmologists, optometrists and allergists; but we have a right of first refusal to obtain such rights in the event Allergan decides to engage a third party to undertake such activities. We have established a joint commercialization committee with Allergan to coordinate and oversee the broad strategies, promotion activities and manage the relationship. Allergan is responsible for supply chain management, managed healthcare, customer order processing and regulatory compliance. Under the terms of the agreement, we paid Allergan an up-front payment and Allergan pays co-promotion revenue to us on U.S. net sales of Elestat™, except in the event that a third party is engaged by Allergan to promote Elestat™ to prescribers outside of our field, in which case we will be paid a proportionate share of U.S. net sales of Elestat™

based upon filled prescriptions written by ophthalmologists, optometrists and allergists. Under the terms of the agreement, we are required to achieve certain performance minimums to receive some or all of co-promotion revenue contemplated.

The agreement will be in effect until the earlier of: (i) the approval and launch of the first generic epinastine product; or (ii) the approval and launch of the first over-the-counter epinastine product; in each case after expiration of the listing of Elestat™ in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (generally known as the "Orange Book"). Either Allergan or we may terminate the agreement in the event of a material breach of the agreement by the other or in the event of the other's insolvency. Allergan can terminate the agreement if we fail to meet a defined minimum of net sales in any given year, or upon a change of control where we become an affiliate of a direct competitor of Allergan's as that term is defined in the agreement. We can terminate the agreement in the event that Elestat™ is withdrawn from the market for more than ninety days.

Allergan, Inc. – Restasis® and diquafosol

In June 2001, we entered into a joint license, development and marketing agreement with Allergan to develop and commercialize diquafosol. The agreement also granted the right to co-promote Restasis® in the United States. In December 2003, at the time we entered into the co-promotion agreement relating to Elestat™, we amended the joint license, development and marketing agreement to reduce the co-promotion revenue rates that we would receive upon the sale of Restasis®.

Under the terms of the amended agreement, Allergan obtained an exclusive license to develop and commercialize diquafosol worldwide, with the exception of Japan and nine other Asian countries covered by our agreement with Santen. In return, we will receive co-promotion revenue from Allergan on net sales of Restasis® and diquafosol, if any, worldwide, excluding most larger Asian markets. In December 2002, Restasis® was approved for sale by the FDA and Allergan launched Restasis® in the United States in April 2003. We began receiving co-promotion revenue on net sales of Restasis® in April 2004, and have received milestone payments under this agreement. In the third quarter of 2003, we exercised our right under the Allergan agreement to co-promote diquafosol and Restasis®. We began promoting Restasis® in January 2004 and will promote diquafosol if and when we receive FDA approval.

We have established a joint development committee with Allergan to oversee the joint development program and a joint commercialization committee to establish the broad strategies and manage the relationship. Under the terms of the agreement, we provide bulk active drug substance while diquafosol is in development and Allergan is responsible for obtaining or manufacturing all of its bulk active drug substance requirements and for commercial supply of product.

We are responsible for conducting, in collaboration with Allergan, the Phase 3 clinical trials for diquafosol for dry eye disease and for United States NDA filing and potential approval. Allergan is responsible for all other development activities under the agreement, including all development outside the United States and in its territories, and for ex-United States regulatory submissions, filings, and approvals relating to products. In addition, all development costs associated with a potential corneal wound healing indication for diquafosol are solely our responsibility until such time, if any, that we receive an NDA approval of diquafosol. Allergan is responsible for all commercial costs except for the cost of our sales force in the United States. Allergan is required to use commercially reasonable efforts to conduct development, seek regulatory approvals and market and sell the products.

The agreement will be in effect until all patents licensed under the agreement have expired. Either Allergan or we may terminate the agreement in the event of a material breach of the agreement. In addition, we have the right to terminate the agreement if we determine, subject to the joint commercialization committee's review and arbitration, that Allergan has not made reasonably sufficient progress in the commercialization of our product by giving 180 days prior notice. If Allergan breaches the agreement, becomes insolvent or we terminate for failure

to make progress with the commercialization of our product, Allergan's license will terminate and Allergan must provide us with all data and information relating to our product and must assign or permit us to cross-reference all regulatory filings and approvals.

Santen Pharmaceutical Co., Ltd.

In December 1998, we entered into a Development, License and Supply Agreement with Santen for the development of diquafosol for the therapeutic treatment of ocular surface diseases, such as dry eye disease and corneal wound healing, in Asia. Under the agreement, we granted Santen an exclusive license to market diquafosol for ocular surface diseases in Japan, China, South Korea, the Philippines, Thailand, Vietnam, Taiwan, Singapore, Malaysia and Indonesia.

We established a coordinating committee to review and evaluate Santen's progress in the development and commercialization of products. Santen is responsible for all development, regulatory submissions, filings and approvals, and all marketing of products. We are obligated to supply Santen with its requirements of diquafosol in bulk drug substance form for all preclinical studies, clinical trials and commercial requirements at agreed-upon prices.

Under the terms of the agreement, we received an up-front equity investment of $1.5 million for shares of our preferred stock in December 1998, that were subsequently converted into shares of our common stock. During 2000, we received a milestone payment under the Santen Agreement of $500,000 based on achievement of a regulatory milestone by Santen. In addition, depending on whether all milestones are met, we could receive additional payments of up to $4.25 million, as well as royalties on net sales of licensed products.

The agreement will terminate when all patents licensed under the agreement have expired. Either Santen or we may terminate the agreement if the other materially breaches the agreement. In addition, we have the right to terminate the agreement at any time if we determine, subject to the coordinating committee's review and arbitration, that Santen has not made reasonably sufficient progress in the development or commercialization of products. If Santen breaches the agreement, or if we terminate the agreement because Santen has not made sufficient progress, Santen's license will terminate. Santen will provide us with all data and information relating to our products, and will assign or permit us to cross-reference all regulatory filings and approvals.

Cystic Fibrosis Foundation Therapeutics, Inc.

In October 2002, we entered into a study funding agreement with the CFFT, a non-profit drug development affiliate of the Cystic Fibrosis Foundation, for the funding of one Phase 2 clinical trial in INS37217 Respiratory for the treatment of cystic fibrosis. Under the agreement, the CFFT provided the majority of funding of external costs for one Phase 2 clinical trial of INS37217 Respiratory in exchange for post-commercialization development and sales milestone payments. The clinical trial was designed in collaboration with the CFFT and the Therapeutics Development Network. In October 2004, we presented detailed results of this clinical trial and we are progressing the clinical development of this product candidate. If the product candidate ultimately receives FDA approval, we would be obligated to pay a development milestone to the CFFT, calculated as a multiple of the clinical trial costs incurred by the CFFT. In addition, we would be obligated to pay a sales milestone if the product candidate achieves a certain aggregate sales volume in the first five years following product approval. The development milestone is currently estimated to be approximately $12 million, payable over five years and the sales milestone would be an additional $4 million, payable over two years.

The agreement will terminate no later than the expiration of all payment obligations under the agreement. Either the CFFT or we may terminate the agreement if the other materially breaches the agreement.

Kirin Brewery Co., Ltd. Pharmaceutical Division

In September 2000, we entered into a License Agreement with Kirin for the development and commercialization of INS316 Diagnostic. Under the agreement we granted Kirin an exclusive license to commercialize INS316 Diagnostic in 21 Asian countries and regions, including Japan. Kirin terminated its license for this drug candidate in September 2004.

License Agreements

The University of North Carolina at Chapel Hill

In March 1995, September 1998, and January 2002, we entered into three separate agreements with UNC granting us exclusive worldwide licenses to develop, make, use and sell products based on UNC patented technology relating to the use of P2Y receptor agonists and antagonists for respiratory therapeutics, such as INS365 Respiratory; respiratory diagnostics, such as INS316 Diagnostic; and prevention of platelet aggregation, such as INS50589. In connection with these license agreements, we have paid an aggregate of $105,000 in license initiation fees and have agreed to pay milestone payments totaling $650,000. In addition, we would be obligated to pay royalties based on net sales of certain licensed products as defined in the agreements. In March 1995, we also entered into a fourth agreement that granted us a non-exclusive worldwide license to use other UNC patented technology as a research tool to identify agonists and antagonists for P2Y receptors.

If we fail to meet performance milestones relating to the timing of regulatory filings or pay the minimum annual payments under our respective UNC licenses, UNC may terminate the applicable license.

Wisconsin Alumni Research Foundation

In November 2004, we licensed several patents for use in developing and commercializing new treatments for glaucoma from Wisconsin Alumni Research Foundation, or WARF. Under the terms of the agreement, we paid an upfront licensing payment of $150,000 and are obligated for additional contingent payments of up to an aggregate of $1.8 million upon the achievement of development milestones, and royalties on sales of any regulatory approved product utilizing the licensed patents.

We will design and fund all future research, development, testing, regulatory filings and potential marketing activities related to any product developed from the license. Unless terminated earlier, the agreement will expire on a country-by-country basis upon the expiration of the patents in such country.

If we fail to meet performance milestones relating to the timing of regulatory filings or pay the minimum annual payments under this license, WARF may terminate the applicable license.

Research and Development

Discovery

Our scientists have specific expertise and proprietary knowledge relating to the design and synthesis of P2 receptor agonists and antagonists, including $P2Y_2$ agonists, $P2Y_{12}$ antagonists and P2X antagonists. We have invested in state-of-the-art equipment and laboratory space for performing synthetic chemistry, determination of compound structure and receptor location and function identification. Our discovery effort is focused on conducting studies using cell-based scientific tests that measure biological activities caused by stimulation or blocking of P2 receptors, to identify new compounds that specifically and selectively bind to members of the P2 receptor family. These tests enable us to identify agonists and antagonists that act at specific receptor subtypes and demonstrate a level of specificity and activity that merits further investigation. We use data from these tests to design and synthesize compounds specific to each P2 receptor subtype that can be advanced to clinical trials.

By screening against several P2 receptor subtypes, we have been able to identify agonists and/or antagonists that interact preferentially with a specific receptor subtype. Several proprietary discovery compounds, including new chemical entities, with promising stability and metabolic profiles are being actively explored. We intend to conduct further preclinical development studies to advance such proprietary compounds to project status, if appropriate. These compounds will then be targeted to the treatment of new disease areas, as identified through our strategic planning process.

Additionally, we are synthesizing compounds that are active as actin cytoskeleton binding agents to discover new treatments for glaucoma. These compounds will be tested in cellular assays and in animal models of intraocular pressure. This research falls under technology licensed from WARF in 2004.

We obtain access to chemical libraries through our own proprietary chemistry, commercial sources and corporate agreements. The chemicals are screened for both agonist and antagonist activity. Our chemistry department also assists in the development of analytical protocols used by contract service organizations for analysis of a drug substance, clinical trial material and drug stability studies which will be incorporated into IND and NDA filings.

We use sponsored research agreements to investigate specific biological processes to augment our technology platform. We have sponsored research agreements at major universities. We use contract research organizations for all toxicology and most animal studies required for regulatory submissions, such as IND applications.

Development

After a molecule is determined to be an appropriate product candidate based upon our research findings and business strategy, it moves into the development function of our organization, where extensive testing of both the characteristics of the actual product and the effects it has on humans are conducted. The progression of products through the various stages of development is overseen by our Portfolio Review Committee, a group comprised of certain company officers and selected senior staff from the Development and Discovery departments. Our development function is divided into four functional areas, Pharmaceutical Development, Regulatory Affairs, Clinical Research, and Biostatistics and Data Management.

When a product candidate is judged as ready for human testing, an IND is filed with the FDA that, upon review, allows us to embark on human testing in the United States. Since 1997, we have filed seven INDs for product candidates that were subsequently evaluated in humans. Some of these product candidates have progressed to later phases of development. In addition to internal resources, we have many collaborations that allow us to perform development activities with a limited number of staff.

See "Management's Discussion and Analysis of Financial Conditions and Results of Operations – Research and Development Expenses."

Sales and Marketing

Beginning in the first quarter of 2004, we initiated commercial operations and began co-promoting Elestat™ and Restasis® to a select audience of high prescribing eye care professionals and allergists. As a Company, we have limited sales and marketing experience, having just completed our first year of sales and marketing activities. We employ 64 territory managers and 6 regional sales directors to provide us with national sales coverage for Elestat™ and Restasis®. We also have a marketing team and a training and operations team to support our commercialization effort. Our small, specialty commercial organization focuses its promotional efforts on ophthalmologists, optometrists and allergists. We believe our focused marketing organization and a specialty sales force can effectively address these audiences and effectively co-promote these products. Eye care professionals account for the majority of the dry eye disease prescriptions and combined with the allergists these specialties prescribe approximately half of the ocular allergies prescriptions. Targeting these medical specialties is an excellent strategic fit for Elestat™ and our dry eye disease product and product candidate, Restasis® and diquafosol.

In the United States, we are co-promoting Elestat™ and Restasis® and intend to co-promote diquafosol if and when that product candidate receives FDA approval. We co-promote Restasis® in the United States with Allergan, but we have primary United States sales and marketing responsibilities for Elestat™. We have not developed commercial plans for our product candidates beyond Elestat™, Restasis® and diquafosol as these plans will be dependent in large part on their market potential and our financial resources. We intend to establish corporate partnering, licensing or other arrangements for the marketing and sale of selected product candidates that we develop, especially outside of North America. We do not intend to develop international

operations outside of North America. Accordingly, third parties may have significant control or influence over important aspects of the commercialization of our product candidates, including market identification, marketing methods, pricing, composition and magnitude of sales force and promotional activities. We may have limited control over the amount and timing of resources that a third party devotes to our products.

We feel the establishment of our commercial operations provides us with the opportunity and flexibility to market and sell other products we are developing, or products that we may in-license or otherwise acquire, and to maximize their commercial value in the United States.

Compliance

We are committed to conducting our business fairly, honestly, ethically and lawfully. We act responsibly and with integrity in our relationships with patients, health care professionals, providers, governments, regulatory entities, customers, suppliers, vendors and stockholders.

We have designated a Corporate Compliance Officer who reports to the Chief Executive Officer and Chairman of the Audit Committee of the Board of Directors. The Corporate Compliance Officer is responsible for evaluating potential compliance risks within the company and designing control procedures. This is achieved by conducting audits consistent with implementation of codes, policies and other controls. Areas of control include, but are not limited to, compliance with current Federal and State law, such as the Sarbanes-Oxley Act of 2002, U.S. Foreign Corrupt Practices Act of 1977, NASDAQ and National Association of Securities Dealers listing requirements and Securities and Exchange Commission, FDA, and Office of Inspector General regulations. Codes and policies that have been implemented include, but are not limited to, "Code Of Ethics and Conduct Relating to Financial Affairs," "Code of Business Ethics," "Whistleblower Policy" and "Code of Conduct: Promotional Interactions with Health Care Professionals." The Corporate Compliance Officer provides frequent updates to senior management, the Audit Committee of the Board of Directors and to the full Board of Directors.

Manufacturing and Supply

We do not currently engage in, nor do we expect to engage in, the manufacture of bulk active pharmaceutical ingredients, or APIs, for preclinical, clinical or commercial purposes. We rely on a contract manufacturing supply arrangement with a single manufacturer located in Choshi, Japan, for the development stage production of diquafosol and INS37217 (denufosol). We expect that this vendor will ultimately supply commercial quantities of these compounds for both ophthalmic and respiratory applications. We have already obtained cGMP grade batches of these compounds and our vendor has completed the validation of the manufacturing process for diquafosol. INS50589, the API for our antiplatelet program, is manufactured by a vendor located in Ontario, Canada. Although we have identified potential alternative sources for our product candidates, we presently depend on these two vendors as the sole manufacturers of APIs for our various programs. See "Risk Factors— Reliance on a single party to manufacture and supply either finished product or the bulk active pharmaceuticals ingredients for a product or product candidates could adversely affect us."

In addition to the bulk APIs, our products incorporate pharmacopeial grade excipients such as sodium chloride, sodium hydroxide and hydrochloric acid, all of which are readily available from numerous sources. Many of our clinical trial materials are packaged in form-fill-seal vials, which are manufactured by a single vendor, but similar vials are also available from other commercial filling and packing companies. In addition to form-fill-seal vial packaging, we also administer our product candidates as intravitreal injections and intravenous infusions. The intravitreal injections and intravenous infusions have been manufactured by a single vendor using standard glass vials and rubber stoppers. In the case of both injection products, alternate sources of both components and manufacturing sites are available.

We have established a Corporate Quality and Compliance function to conduct qualification and routine audits of our contract manufacturers. These contract manufacturers are identified in our regulatory agency filings,

such as with the FDA, and are subject to Regulatory Agency Inspections. We also attempt to stay informed on the financial condition of contract manufacturers and their status with regulatory agencies. Although we also maintain an inventory of drug product in order to minimize the risk of material shortage, a prolonged interruption in supply could adversely disrupt our manufacturing plans.

The manufacture of our products and product candidates is based in part on technology that we believe to be proprietary to our contract manufacturers or our collaborative partners. Such manufacturers may not abide by the limitations or confidentiality restrictions in agreements with us. In addition, any such manufacturer may develop process technology related to the manufacture of our compounds that such supplier owns either independently or jointly with us. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have our products manufactured.

Patents and Proprietary Rights

We believe that the proprietary protection of our product candidates, processes and know-how is important to the success of our business. We aggressively file and prosecute patents covering our proprietary technology and, if warranted, will defend our patents and proprietary technology. As of January 31, 2005, we owned or licensed patent rights consisting of 48 issued United States patents, none of which expire before 2011, and numerous pending applications in the United States and corresponding patents and patent applications in foreign jurisdictions. We seek patent protection for our proprietary technology and products in the United States and Canada and in key commercial European and Asia/Pacific countries and other major commercial sectors of the world, as appropriate. We intend to seek trademark protection in the United States and foreign countries, as appropriate. We also rely upon trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain our competitive position.

In March 1995, September 1998, and January 2002, we entered into three separate agreements with UNC granting us exclusive worldwide licenses to develop, make, use and sell products based on UNC patented technology relating to the use of P2Y receptor agonists and antagonists for respiratory therapeutics, such as INS365 Respiratory; respiratory diagnostics, such as INS316 Diagnostic; and prevention of platelet aggregation, such as INS50589. The term of each of the UNC exclusive licenses is based upon the duration of the patents covered by each of these agreements. The United States government may have limited rights in some of this UNC patented technology. The agreements require us to pay licensing fees upon the attainment of development milestones and royalties on net sales or a share of sublicensing income on products covered by the patents. We are also required to meet due diligence milestones and UNC may terminate the licenses if we fail to do so. In March 1995, we also entered into a fourth agreement that granted us a non-exclusive worldwide license to use other UNC patented technology as a research tool to identify agonists and antagonists for P2Y receptors.

In November 2004, we entered into an agreement with WARF granting us an exclusive license to develop, make, have made, use, market, distribute, import, offer for sale, and sell products based on WARF patented technology relating to the treatment of ocular diseases. The term of the exclusive license from WARF is based upon the duration of the patents covered by this agreement. The United States government may have limited rights in some of this patented technology. We are also required to meet due diligence milestones and WARF may terminate the license if we fail to do so.

Additional patent applications have been filed on discoveries made in support of the UNC technologies, from research conducted at UNC or in our own laboratories. Our sponsored research agreements, material transfer agreements, and other collaborations have the potential to result in license agreements with universities, institutions and businesses. We believe that our patents and licensed patents provide a substantial proprietary base that will allow us, and our collaborative partners, to exclude others from conducting our business as described in this report and as encompassed by our issued patents and issued patents licensed to us. We cannot be sure, however, that pending or future applications will issue, that the claims of any patents which do issue will provide any significant protection of our technology or that our directed discovery research will yield compounds and products of therapeutic and commercial value.

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

Competition

Many pharmaceutical companies engage in research and development to commercialize products to treat allergic conjunctivitis, dry eye disease, cystic fibrosis, and other diseases that we are researching. We compete with these companies for funding, access to licenses, personnel, third party collaborators and product development. Most of these companies have substantially greater financial, marketing, sales, distribution and technical resources and more experience in research and development, clinical trials and regulatory matters, than we do. We are aware of existing treatments that will compete with our products.

We believe that several major pharmaceutical companies have initiated research programs to design P2Y receptor agonists or antagonists. However, we are not aware of any competing $P2Y_2$ receptor agonists that have entered clinical testing. If successfully developed and commercialized, our products will compete with existing therapeutics and any new treatments developed by competitors.

There are multiple therapies available to treat or prevent allergic conjunctivitis. The primary brands that Elestat™ competes with are Patanol®, Zaditor® and Optivar®. Patanol® currently has the majority of the prescriptions in the allergic conjunctivitis market.

The current prescription and non-prescription treatments for dry eye disease include artificial tear replacement therapy or lubricant eye drops. The FDA approved Restasis® in December of 2002 for patients with dry eye disease whose tear production is presumed to be suppressed due to ocular inflammation. We are aware of the following dye eye disease pharmaceutical products in clinical development: 15-HETE and rimexolone, by Alcon, Inc.; OPC-12759 (rebamipide), by Otsuka Pharmaceuticals, licensed to Novartis; Ecabet sodium by ISTA Pharmaceuticals, licensed from Senju; ProGraf/FK-506, by Fujisawa Healthcare, Inc.; pimecrolimus by Novartis; and Androgen Tears, by Allergan. We are not aware of any other pharmaceutical approved products or product candidates in clinical development for corneal wound healing.

There are two products approved in the United States specifically for the treatment of complications of cystic fibrosis: Pulmozyme®, an agent designed to break up thickened airway secretions, and TOBI®, an inhaled antibiotic. At least one clinical trial has been completed that demonstrated clinical benefit with Zithromax®, an oral antibiotic. Although Zithromax® has not been officially approved by the FDA for use in cystic fibrosis, it has been added to the treatment regimen in patients with evidence of airway infection. In addition, Corus Pharma, Inc. is developing aztreonam via inhalation as a therapy for cystic fibrosis.

We are not aware of any other pharmaceuticals treatments available for retinal detachment, but some pharmaceutical companies have product candidates focused on macular edema.

Plavix® is an approved platelet aggregation inhibitor that irreversibly inhibits the $P2Y_{12}$ receptor on platelets. There are two additional $P2Y_{12}$ receptor antagonists in clinical development as platelet aggregation inhibitors. Cangrelor (The Medicines Company) has finished Phase 2 clinical testing using intravenous administration. AZD6140 (AstraZeneca) is in Phase 2 clinical testing and is an oral formulation.

The introduction of new products or the development of new processes by competitors or new information about existing products may result in price reductions or product replacements, even for products protected by patents. However, we believe our competitive position is enhanced by our commitment to research leading to the

discovery and development of new products. Other factors that may help us meet competition include the quality and breadth of our technology platform, the skill of our employees and our ability to recruit and retain skilled employees, our aggressive program of seeking patent protection and our capabilities for early stage research and drug discovery. However, many large pharmaceutical and biotechnology companies have significantly larger intellectual property estates than we do, more substantial capital resources than we have and greater capabilities and experience than we do in preclinical and clinical development, sales, marketing, manufacturing and regulatory affairs.

Governmental Regulation

The research, development, testing, manufacture, promotion, marketing and distribution of human therapeutic and diagnostic products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs and diagnostic products and similar regulatory bodies exist in other countries. The steps ordinarily required before a new drug may be marketed in the United States, which are similar to steps required in most other countries, include:

- Preclinical laboratory tests, preclinical studies in animals and formulation studies and the submission to the FDA of an IND for a new drug;
- Adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication;
- The submission of an NDA to the FDA; and
- FDA review and approval of the NDA before any commercial sale or shipment of the drug.

Preclinical tests include laboratory evaluation of product toxicity and formulation, as well as animal studies. The results of preclinical testing are submitted to the FDA as part of an IND. A 30-day waiting period after the filing of each IND is required before the commencement of clinical testing in humans. At any time during this 30-day period or later, the FDA may halt proposed or ongoing clinical trials until the FDA authorizes trials under specified terms. The IND process may be extremely costly and substantially delay development of our products. Moreover, positive results of preclinical tests will not necessarily indicate positive results in clinical trials.

Clinical trials to support NDAs are typically conducted in three sequential phases, but the phases may overlap. During Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics and pharmacological actions and safety, including side effects associated with increasing doses. Phase 2 usually involves studies in a limited patient population to:

- Assess the efficacy of the drug in specific, targeted indications;
- Assess dosage tolerance and optimal dosage; and
- Identify possible adverse effects and safety risks.

If a compound is found to be potentially effective and to have an acceptable safety profile in Phase 2 evaluations, Phase 3 trials, also called pivotal studies, major studies or advanced clinical trials, are undertaken to further demonstrate clinical efficacy and to further test for safety within an expanded patient population at geographically dispersed clinical trial sites.

After successful completion of the required clinical testing, generally a NDA is submitted. The FDA may request additional information before accepting a NDA for filing, in which case the application must be resubmitted with the additional information. Once the submission has been accepted for filing, the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA to an appropriate advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by the recommendation of an advisory committee.

If FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may give us either an approval letter or an approvable letter. An approvable letter will usually contain a number of conditions that must be met, which may include additional testing, in order to secure final approval of the NDA and authorization of commercial marketing of the drug for particular indications; however, the receipt of an approvable letter does not guarantee the final approval of a product. The FDA may refuse to approve the NDA or give us a non-approvable letter, outlining the deficiencies in the submission. If regulatory approval of a product is granted, it will be limited to particular disease states or conditions.

We and any of our contract manufacturers are also required to comply with the applicable FDA cGMP regulations. Good manufacturing practice regulations include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Manufacturing facilities are subject to inspection by the FDA. These facilities must be approved before we can use them in commercial manufacturing of our products. Our contract manufacturers or we may not be able to comply with the applicable good manufacturing practice requirements and other FDA regulatory requirements.

Outside the United States, our ability to market our products will also depend on our receipt of marketing authorizations from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials and marketing authorization vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Union procedures are available to companies wishing to market a product in more than one member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, a marketing authorization will be granted. This foreign regulatory approval process, including those in Europe and Japan, involves all of the risks associated with FDA clearance discussed above.

Health Care Reform Measures and Third Party Reimbursement

The efforts of governments and third party payors to contain or reduce the cost of health care will continue to affect the business and financial condition of drug companies. A number of legislative and regulatory proposals to change the health care system have been considered in recent years. In addition, an increasing emphasis on managed care in the United States has and will continue to increase pressure on drug pricing. Legislative or regulatory proposals or changes in managed care systems may be adopted that may have a negative effect on our business. The announcement and/or adoption of proposals could have an adverse effect on our ability to earn profits and financial condition. Sales of prescription drugs depend significantly on the availability of reimbursement to the consumer from third party payors, such as government and private insurance plans. These third party payors frequently require that drug companies give them predetermined discounts from list prices and they are increasingly challenging the prices for medical products and services. Third party payors may not consider products we may bring to the market cost effective and may not reimburse the consumer sufficiently to allow us, and/or our collaborators, to sell our products on a profitable basis.

Employees

As of January 31, 2005, we had 165 full-time and part-time employees. In addition, we utilize interns, outside contractors and consultants as needed. Our future success will depend in large part upon our ability to attract and retain highly qualified personnel. Our employees are not represented by any collective bargaining agreements, and we have never experienced a work stoppage. Employees are required to execute confidentiality and assignment of intellectual property agreements.

Internet Information

Our internet site is located at www.inspirepharm.com. Copies of our reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act, including annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports may be accessed from our website, free of charge, as

soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission. Please note that the information contained on our website is not incorporated by reference into our reports that are filed with the SEC.

We file our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 electronically with the Securities and Exchange Commission, or the SEC. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 450 Fifth Street, NW, Washington DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is www.sec.gov.

RISK FACTORS

An investment in the shares of our common stock involves a substantial risk of loss. You should carefully read this entire report and should give particular attention to the following risk factors. You should recognize that other significant risks may arise in the future, which we cannot foresee at this time. Also, the risks that we now foresee might affect us to a greater or different degree than expected. There are a number of important factors that could cause our actual results to differ materially from those indicated by any forward-looking statements in this document. These factors include, without limitation, the risk factors listed below and other factors presented throughout this document and any other documents filed by us with the Securities and Exchange Commission.

If the FDA does not conclude that our product candidates meet statutory requirements for safety and efficacy, we will be unable to obtain regulatory approval for marketing in the United States, and if foreign governments do not conclude that our product candidates meet their requirements for marketing, we will be unable to sell those product candidates in those foreign markets.

To achieve profitable operations, we must, alone or with others, successfully identify, develop, introduce and market proprietary products. We have not received marketing approval for any of our product candidates, although we are co-promoting two products with Allergan. We have one product candidate, diquafosol, for which we have received an approvable letter from the FDA. Since the initial submission of our NDA for diquafosol, we have completed two additional diquafosol Phase 3 clinical trials, trials 108 and 109. Although neither of the two additional diquafosol Phase 3 clinical trials met their primary endpoint, we plan to submit an amendment to our diquafosol NDA by June 30, 2005 based upon the totality of data from our diquafosol clinical program, including positive data on certain secondary endpoints and analyses from the 108 and 109 clinical trials. There is no guarantee that the FDA will approve diquafosol and allow Allergan and us to begin selling it in the United States based on the totality of such data. It may be necessary to undertake additional Phase 3 clinical trials in support of our diquafosol NDA and there can be no guarantee that any such additional clinical trials would be successful or that the FDA would approve diquafosol even if such additional clinical trials are successful. Also, if additional diquafosol Phase 3 clinical trials are required by the FDA, we may decide not to conduct those clinical trials and we would therefore be unable to obtain FDA approval of diquafosol. Even if we do receive FDA approval for diquafosol, we and Allergan may not be able to successfully commercialize diquafosol in the United States. We have not applied for marketing approval of diquafosol in any other jurisdiction.

In addition to our product candidates in clinical development, we have early stage preclinical product candidates for which a substantial amount of work will be required to advance these product candidates to clinical testing and ultimately to commercial approval. We will have to conduct significant additional development activities, non-clinical and clinical tests and obtain regulatory approval before our product candidates can be commercialized. Product candidates that may appear to be promising at early stages of development may not successfully reach the market for a number of reasons. The results of preclinical and initial clinical testing of our product candidates under development may not necessarily indicate the results that will be obtained from later or more extensive testing. Accordingly, some preclinical candidates may not advance to clinical development. Additionally, companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. Our ongoing clinical trials might be delayed or halted for various reasons, including:

- The drug is not effective or physicians think that the drug is not effective;
- The drug effect is not statistically significant compared to placebo;
- Patients experience severe side effects during treatment;
- Patients die during the clinical trial because their disease is too advanced or because they experience medical problems that may or may not relate to the drug being studied;
- Patients do not enroll in the clinical trials at the rate we expect;

- We decide to modify the drug during testing; or
- We allocate our limited financial and other resources to other clinical programs.

The introduction of our products in foreign markets will subject us to foreign regulatory clearances, the receipt of which may be unpredictable and uncertain, and which may impose substantial additional costs and burdens which we or our partners in such foreign markets may be unwilling or unable to pay. As with the FDA, foreign regulatory authorities must be satisfied that adequate evidence of safety, quality and efficacy of the product has been presented before marketing authorization is granted. The foreign regulatory approval process includes all of the risks associated with obtaining FDA marketing approval. Approval by the FDA does not ensure approval by other regulatory authorities.

Failure to successfully market and commercialize Restasis® and Elestat™ will limit our revenues.

Allergan launched Restasis® in the United States in April 2003 and we began receiving co-promotion revenue from Allergan on the net sales of Restasis® beginning in April 2004. Although our agreement with Allergan provides, and we have exercised, the right to co-promote Restasis® in the United States; Allergan is primarily responsible for marketing and commercializing Restasis®. Accordingly, our revenues on the net sales of Restasis® are largely dependent on the actions and success of Allergan, over whom we have no control.

In February 2004, we launched Elestat™ in the United States. Our agreement with Allergan provides that we will have the primary responsibility for selling, promotional and marketing activities related to Elestat™ in the United States. We are required to pay the costs in relation to such activities. We expect selling, promotional and marketing expenses associated with Elestat™ and Restasis® will exceed the corresponding revenues derived from these products during the year ending December 31, 2005 and there can be no assurances that revenues associated with such products will ever exceed the related expenses.

In December 2004, Alcon, Inc. received FDA approval of once-daily olopatadine hydrochloride ophthalmic solution, a product which directly competes with Elestat™. To the best of our knowledge, Alcon has not yet launched once-daily olopatadine hydrochloride ophthalmic solution, but Patanol® (olopatadine hydrochloride ophthalmic solution) that requires administration twice-a-day currently competes with Elestat™. We cannot predict what effect, if any, the introduction of once-daily olopatadine hydrochloride ophthalmic solution will have on our sales of Elestat™.

Until our launch of Elestat™ and co-promotion of Restasis®, we had never been involved in the promotion or co-promotion of a product. Our future revenues will depend, in part, upon the acceptance of Elestat™ and Restasis® by eye-care professionals, allergists and patients. Factors that could affect the acceptance of Elestat™ and Restasis® include:

- Satisfaction with existing alternative therapies;
- Regulatory approval in other jurisdictions;
- Perceived efficacy relative to other available therapies;
- Effectiveness of our sales and marketing efforts;
- Effectiveness of Allergan's sales and marketing efforts;
- Changes in, or the levels of, third-party reimbursement of product costs;
- Cost of treatment;
- Marketing and sales activities of competitors;
- Pricing and availability of alternative products;

- Shifts in the medical community to new treatment paradigms or standards of care;
- Relative convenience and ease of administration; and
- Prevalence and severity of adverse side effects.

We cannot predict the potential long-term patient acceptance of, or the effects of competition and managed health care on, sales of either product.

Revenues in future periods could vary significantly and may not cover our operating expenses.

We recognize revenue from product co-promotion based on net sales for Elestat™ and Restasis® as defined in the co-promotion agreements and as reported to us by our collaborative partner, Allergan. Accordingly, our co-promotion revenue is based upon Allergan's revenue recognition policy, other accounting policies and the underlying terms of our co-promotion agreements. We recognize milestone revenue under our collaborative research and development agreements when we have performed services under such agreements or when we or our collaborative partner has met a contractual milestone triggering a payment to us. We did not reach any such milestones in 2004 and there can be no assurances that we will reach any during the year ended December 31, 2005 or any later date. Revisions in the commitment period are made in the period that the facts related to the change first become known. Additionally, our revenues may fluctuate from period to period due in part to:

- Fluctuations in sales of Elestat™, Restasis® and other future licensed or co-promoted products due to competition, manufacturing difficulties, seasonality, or other factors that affect the sales of a product;
- The timing of approvals, if any, for future products;
- The progress toward and the achievement of developmental milestones by us or our partners;
- Fluctuations in foreign currency exchange rates;
- The initiation of new contractual arrangements with other companies;
- The failure or refusal of a collaborative partner to pay royalties; or
- The expiration or invalidation of our patents or licensed intellectual property.

Failure to adequately market and commercialize diquafosol, if approved by the FDA, will limit our revenues.

If approved by the FDA and other applicable regulatory authorities outside the United States, the commercial success of diquafosol will largely depend on the scope of the launch into the United States and other major pharmaceutical markets, acceptance by patients and eye care professionals and allergists, ongoing promotional activities, a knowledgeable sales force and adequate market penetration. In the event diquafosol is approved by the FDA, we plan to co-promote diquafosol within the United States; however, Allergan is primarily responsible for marketing diquafosol in the United States and other major, ex-Asia pharmaceutical markets. If diquafosol is not successfully commercialized, our revenues will be limited.

We cannot sell Restasis®, Elestat™ or any of our product candidates if governmental approvals are not obtained and maintained.

Pharmaceutical companies are subject to significant regulation by a number of national, state and local agencies, including the FDA. Failure to comply with applicable regulatory requirements could, among other things, result in fines, suspensions of regulatory approvals of products, product recalls, delays in product distribution, marketing and sale, and civil or criminal sanctions.

The manufacturing and marketing of drugs, including our products, are subject to continuing FDA and foreign regulatory review, and later discovery of previously unknown problems with a product, manufacturing

process or facility may result in restrictions, including withdrawal of the product from the market. The FDA is permitted to revisit and change its prior determinations and it may change its position with regard to the safety or effectiveness of our products. The FDA is authorized to impose post-marketing requirements such as:

- Testing and surveillance to monitor the product and its continued compliance with regulatory requirements;
- Submitting products for inspection and, if any inspection reveals that the product is not in compliance, the prohibition of the sale of all products from the same lot;
- Suspending manufacturing;
- Recalling products; and
- Withdrawing marketing approval.

Even before any formal regulatory action, we, or our collaborative partners, could voluntarily decide to cease distribution and sale or recall any of our products if concerns about safety or effectiveness develop.

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

- Incur substantial expenses, including fines, penalties, legal fees and costs to comply with the FDA's requirements;
- Change our methods of marketing and selling products;
- Take FDA-mandated corrective action, which could include placing advertisements or sending letters to physicians rescinding previous advertisements or promotion; or
- Disrupt the distribution of products and stop sales until we are in compliance with the FDA's position.

In recent years, various legislative proposals have been offered in Congress and in some state legislatures that include major changes in the health care system. These proposals have included price or patient reimbursement constraints on medicines and restrictions on access to certain products. We cannot predict the outcome of such initiatives and it is difficult to predict the future impact of the broad and expanding legislative and regulatory requirements affecting us.

Recent Medicare prescription drug coverage legislation and future legislative or regulatory reform of the healthcare system may affect our or our partner's ability to sell products profitably.

In both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our ability to sell our products profitably. In the United States, in December 2003, President Bush signed into law new Medicare prescription drug coverage legislation. Part of the legislation authorizes the Centers for Medicare & Medicaid Services, or CMS, the agency within the Department of Health and Human Services that administers Medicare to implement a new Medicare Part D coverage benefit for prescription drugs. Not all drugs in a class may be covered. Further, payment levels under the new Medicare program may be lower than current payment. Medicare patients will have to pay co-insurance which may influence which products are recommended by physicians and selected by patients. There is no assurance that our drugs will be recognized under the new Medicare Part D program for outpatient prescription drugs or paid at levels that reflect current or historical levels. Further federal Medicare proposals, along with State Medicaid drug payment changes and healthcare reforms could also lower payment for our products. Our results of operations could be materially adversely affected by the reimbursement changes emerging in 2006 and 2007 from the Medicare prescription drug coverage legislation. To the extent that private insurers such as Blue Cross and Blue Shield or managed care programs follow Medicare coverage and payment

developments, the adverse effects of lower Medicare payment may be magnified by private insurers adopting lower payment. New Federal or state legislation in the United States may be enacted or adopted in the future that could further lower payment for our products.

Failure to adequately control compliance with all applicable regulations may adversely affect our business.

There are extensive state, federal and foreign regulations applicable to public pharmaceutical companies engaged in the discovery, development and commercialization of medicinal products. There are laws that govern areas including financial controls, testing, manufacturing, labeling, safety, packaging, shipping, distribution and promotion of pharmaceuticals. While we have implemented corporate quality, ethics and compliance programs based on current best practices, we cannot guarantee against all possible transgressions. The potential ramifications are far-reaching if there are areas identified as out of compliance by regulatory agencies including, but not limited to, significant financial penalties, manufacturing and clinical trial consent decrees, commercialization restrictions or other restrictions and litigation.

The Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, and provisions of the Public Company Accounting and Oversight Board require public companies to review, document and test internal controls to ensure that procedures are effective in timely providing management with material information which needs to be disclosed under the Securities Exchange Act of 1934. Our Chief Compliance Officer, our principal executive officers, other management, as well as consultants conducted an evaluation of our internal controls in accordance with Sarbanes-Oxley requirements. As a result of this evaluation, we have provided a management report on our internal controls over financial reporting. However, we can not be sure that we have addressed all control activities and risks or that our overall control structure will detect all reportable events now or in the future.

Since our clinical candidates utilize a new mechanism of action and in some cases there are no regulatory precedents, conducting clinical trials and obtaining regulatory approval may be difficult, expensive and prolonged, which would delay any marketing of our products.

To complete successful clinical trials, our candidates must meet the criteria established for clinical endpoints, which we establish in the clinical trial. Generally, we will establish these endpoints in consultation with the FDA, and other regulatory authorities, following their clinical trial design guidelines on the efficacy, safety and tolerability measures required for approval of products. However, since our product candidates are based on our receptor technology, and some of the diseases we are researching do not have products that have been approved by the FDA, the FDA may not have established guidelines for the design of our clinical trials and may take longer than average to consider our product candidates for approval. The FDA could change its view on clinical trial design and establishment of appropriate standards for efficacy, safety and tolerability and require a change in clinical trial design, additional data or even further clinical trials before granting approval of our product candidates. We could encounter delays and increased expenses in our clinical trials if the FDA determines that the endpoints established for a clinical trial do not predict a clinical benefit. To the best of our knowledge, no $P2Y_2$ products have received marketing approval from the FDA.

After initial regulatory approval, the FDA continues to review a marketed product and its manufacturer. The FDA may require us or our partners to conduct long-term safety studies after approval. Discovery of previously unknown problems through adverse event reporting may result in restrictions on the product, including withdrawal from the market. Additionally, we and our officers and directors could be subject to civil and criminal penalties as a result of such problems.

Projected development costs are difficult to estimate and may change frequently prior to regulatory approval.

While all new compounds require standard regulated phases of testing, the actual type and scope of testing can vary significantly among different product candidates which may result in significant disparities in total costs required to complete the respective development programs.

The number and type of studies that may be required by the FDA, or other regulatory authorities, for a particular compound are based on the compound's clinical profile compared to existing therapies for the targeted patient population. Factors that affect the costs of a clinical trial include:

- The number of patients required to participate in clinical trials to demonstrate statistical significance for a drug's safety and efficacy;
- The time required to enroll the targeted number of patients in clinical trials, which may vary depending on the size and availability of the targeted patient population and the perceived benefit to the clinical trial participants; and
- The number and type of required laboratory tests supporting clinical trials.

Other activities required before submitting a NDA include regulatory preparation for submission, biostatistical analyses, scale-up synthesis, and validation of commercial product. In addition, prior to product launch, production of a certain amount of commercial grade drug product inventory meeting FDA cGMP standards is required.

Also, ongoing development programs and associated costs are subject to frequent, significant and unpredictable changes due to a number of factors, including:

- Data collected in preclinical or clinical trials may prompt significant changes or enhancements to an ongoing development program;
- The FDA may direct the sponsor to change or enhance its ongoing development program based on developments in the testing of similar compounds or related compounds;
- Unexpected regulatory requirements or interim reviews by regulatory agencies may cause delays or changes to development programs; and
- Anticipated manufacturing costs may change significantly due to required changes in manufacturing processes, variances from anticipated manufacturing process yields or changes in the cost and/or availability of starting materials.

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

We have used substantial amounts of cash to fund our research and development activities. Our operating expenses exceeded $56.5 million in the fiscal year ended December 31, 2004, $37.4 million in the fiscal year ended December 31, 2003 and $30.3 million in the fiscal year ended December 31, 2002. We anticipate that our operating expenses in 2005 will increase from our 2004 operating expenses to provide for clinical trials and toxicology studies for INS37217 Respiratory, INS37217 Ophthalmic and INS50589 Antiplatelet and greater commercial and administrative activities. Our cash, cash equivalents and investments totaled approximately $156.8 million on December 31, 2004. We expect that our capital and operating expenditures will continue to exceed our revenue over the next several years as we conduct our research and development activities, clinical trials and undertake commercial sales. Many factors will influence our future capital needs. These factors include:

- The progress of our research programs, including our research program relating to our license agreement with the WARF and our payment obligations thereunder;
- The number and breadth of these research and development programs;
- The size and scope of our marketing programs;
- Our ability to attract collaborators for our products and establish and maintain those relationships;
- Achievement of milestones under our existing collaborations with Allergan and Santen and any future collaborative programs;

- Progress by our collaborators;
- The level of activities relating to commercialization of our products;
- Competing technological and market developments;
- The costs involved in defending any litigation claims against us;
- The costs involved in enforcing patent claims and other intellectual property rights; and
- The costs and timing of regulatory approvals.

In addition, our capital requirements will depend upon:

- The receipt of revenue from Allergan on net sales of Elestat™ and Restasis®;
- The receipt of milestone payments from collaborative agreements;
- Our ability to obtain approval from the FDA for our first product candidate, diquafosol;
- Upon any such approval, our ability together with the ability of our marketing partner, Allergan, to generate sufficient sales of diquafosol; and
- Future potential revenue from Santen and payments from future collaborators.

In the event that we do not receive timely regulatory approvals, we may need substantial additional funds to fully develop, manufacture, market and sell all of our other potential products and support our co-promotion efforts. We may seek such additional funding through public or private equity offerings and debt financings. Additional financing may not be available when needed. If available, such financing may not be on terms favorable to us or our stockholders. Stockholders' ownership will be diluted if we raise additional capital by issuing equity securities. If we raise funds through collaborations and licensing arrangements, we may have to give up rights to our technologies or product candidates which are involved in these future collaborations and arrangements or grant licenses on unfavorable terms. If adequate funds are not available, we would have to scale back or terminate research programs and product development and we may not be able to successfully commercialize any product candidate.

Clinical trials may take longer to complete and cost more than we expect, which would adversely affect our ability to commercialize product candidates and achieve profitability.

Clinical trials are lengthy and expensive. They require adequate supplies of drug product and sufficient patient enrollment. Patient enrollment is a function of many factors, including:

- The size of the patient population;
- The nature of the protocol;
- The proximity of patients to clinical sites;
- The eligibility criteria for the clinical trial; and
- The perceived benefit of participating in a clinical trial.

Delays in patient enrollment can result in increased costs and longer development times. For example, enrollment in our Phase 2 clinical trial for INS37217 Ophthalmic has progressed at a significantly slower rate than originally anticipated and will extend the development time anticipated for this product candidate. Even if we successfully complete clinical trials, we may not be able to submit any required regulatory submissions in a timely manner and we may not receive regulatory approval for the product candidate. In addition, if the FDA or foreign regulatory authorities require additional clinical trials we could face increased costs and significant development delays.

From time to time, we conduct clinical trials in different countries around the world and are subject to the risks and uncertainties of doing business internationally. Disruptions in communication and transportation, changes in governmental policies, civil unrest and currency exchange rates may affect the time and costs required to complete clinical trials in other countries.

Changes in regulatory policy or new regulations could also result in delays or rejection of our applications for approval of our product candidates. Product candidates designed as "fast track" products by the FDA may not continue to qualify for expedited review. Even if some of our product candidates receive "fast track" designation, the FDA may not approve them at all or any sooner than other product candidates that do not qualify for expedited review.

Our common stock price has been highly volatile and your investment in our stock may decline in value.

The market price of our common stock has been highly volatile. These fluctuations create a greater risk of capital losses for our stockholders as compared to less volatile stocks. Factors that have caused volatility and could cause additional volatility in the market price of our common stock include among others:

- Announcements regarding our NDA or foreign regulatory equivalent submissions;
- Announcements made by us concerning results of our clinical trials with diquafosol, INS37217 Respiratory, INS37217 Ophthalmic, INS50589 Antiplatelet and any other product candidates;
- Market acceptance and market share of products we co-promote;
- Volatility in other securities including pharmaceutical and biotechnology securities;
- Changes in government regulations;
- Regulatory actions;
- Changes in the development priorities of our collaborators that result in changes to, or termination of, our agreements with such collaborators, including our agreements with Allergan and Santen;
- Developments concerning proprietary rights including patents by us or our competitors;
- Variations in our operating results;
- Terrorist attacks;
- Military actions; and
- Litigation.

Extreme price and volume fluctuations occur in the stock market from time to time that can particularly affect the prices of biotechnology companies. These extreme fluctuations are sometimes unrelated to the actual performance of the affected companies.

We have been named as a defendant in litigation that could result in substantial damages and costs and divert management's attention and resources

On February 15, 2005, a purported class action complaint was filed in the United States District Court for the Middle District of North Carolina by Mirco Investors, LLC on behalf of itself and all other similarly situated investors against us and certain of our senior officers. The complaint alleges violations of sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Securities and Exchange Commission Rule 10b-5, and focuses on statements that are claimed to be false and misleading regarding a Phase 3 clinical trial of our dry eye product candidate, diquafosol. The plaintiffs seek unspecified damages on behalf of a purported class of purchasers of our securities during the period from June 2, 2004 through February 8, 2005. On February 16, 2005, a similar complaint against the same defendants was filed by Richard and Susan Giorgino. In addition, on March 4, 2005, a similar complaint against the same defendants was filed by Kiah Sai Tan. It is possible that additional

complaints may be filed in the future. We expect that these individual lawsuits will be consolidated into a single civil action. We intend to defend the litigation vigorously. No assurance can be made that we will be successful in our defense of the pending claims. If we are not successful in our defense of the claims, we could be forced to, among other ramifications, make significant payments to resolve the claims and such payments could have a material adverse effect on our business, financial condition and results of operations if not covered by our insurance carriers or if damages exceed the limits of our insurance. Furthermore, regardless of our success in defending against the litigation, the litigation itself may result in substantial costs, use of resources and divert the attention of management and other employees which could adversely affect our business.

If we continue to incur operating losses for a period longer than anticipated, or in an amount greater than anticipated, we may be unable to continue our operations.

We have experienced significant losses since inception. We incurred net losses of $44.1 million for the year ended December 31, 2004, $31.4 million for the year ended December 31, 2003 and $24.7 million for the year ended December 31, 2002. As of December 31, 2004, our accumulated deficit was approximately $171.2 million. We expect to incur significant operating losses over the next several years and expect that cumulative losses may increase in the near-term due to expanded research and development efforts, preclinical studies, clinical trials and commercialization efforts. We expect that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial. Such fluctuations will be affected by the following:

- Timing of regulatory approvals and commercial sales of our product candidates and any co-promotion products;
- The level of patient demand for our products and any licensed products;
- Timing of payments to and from licensors and corporate partners;
- Timing of investments in new technologies and commercial capability;
- Commercialization activities to support co-promotion efforts; and
- The costs involved in defending any litigation claims against us.

To achieve and sustain profitable operations, we must, alone or with others, develop successfully, obtain regulatory approval for, manufacture, introduce, market and sell our products. The time frame necessary to achieve market success is long and uncertain. We may not generate sufficient product revenues to become profitable or to sustain profitability. If the time required to achieve profitability is longer than we anticipate, we may not be able to continue our business.

If we fail to reach milestones or to make annual minimum payments or otherwise breach our obligations under our license agreements, our licensors may terminate our agreements with them.

We hold licenses for INS365 for respiratory diseases and a $P2Y_{12}$ receptor program for a cardiovascular indication from UNC. We also hold a license agreement for glaucoma technologies from WARF. If we fail to meet performance milestones relating to the timing of regulatory filings or fail to pay the minimum annual payments under our respective licenses, our licensors may terminate the applicable license. In addition, if any licensor were to re-license some or all of the technologies currently covered by our licenses, competitors could develop products that compete with ours.

It may be necessary in the future for us to obtain additional licenses to avoid infringement of third party patents. Additionally, we may enter into license arrangements with other third parties as we build our product portfolio. We do not know the terms on which such licenses may be available, if at all.

Reliance on a single party to manufacture and supply either finished product or the bulk active pharmaceutical ingredients for a product or product candidates could adversely affect us.

Under our agreements with Allergan, Allergan is responsible for the manufacture and supply of Elestat™ and Restasis®. It is our understanding that Allergan relies upon an arrangement with a single third party for the

manufacture and supply of APIs for both Elestat™ and Restasis®. Allergan then completes the manufacturing process to yield finished product. In the event such third party was unable to supply Allergan, or Allergan was unable to complete the manufacturing cycle, sales of the product could be adversely impacted, which would result in a reduction in any revenue from product co-promotion received under our agreements with Allergan.

In addition, we have relied upon supply agreements with third parties for the manufacture and supply of the bulk APIs for our product candidates for purposes of preclinical testing and clinical trials. We presently depend upon one vendor as the sole manufacturer of our supply of APIs for diquafosol and INS37217 (denufosol) and one vendor as the sole manufacturer for INS50589. We intend to contract with these vendors, as necessary, for commercial scale manufacturing of our products where we are responsible for such activities. In the case of diquafosol, we expect Allergan to purchase commercial quantities of bulk APIs from our sole manufacturer. Although we have identified alternate sources for our product candidates, it would be time consuming and costly to qualify these sources. Under our diquafosol agreement, either our vendor or we may terminate our supply arrangement, without cause, by giving 180 days prior notice. If our vendor were to terminate our arrangement or fail to meet our supply needs we might be forced to delay our development programs and/or be unable to supply products to the market which could delay or reduce revenues and result in loss of market share.

If we are unable to contract with third parties for the synthesis of APIs required for preclinical testing, for the manufacture of drug products for clinical trials, or for the large-scale manufacture of any approved products, we may be unable to develop or commercialize our drug products.

We have no experience or capabilities to conduct the large-scale manufacture of any of our product candidates. We do not currently expect to engage directly in the manufacturing of drug substance or drug products, but instead intend to contract with third parties to accomplish these tasks. With the exception of Santen, for which we are required to supply bulk APIs, all of our partners are responsible for making their own arrangements for the manufacture of drug products, including arranging for the manufacture of bulk APIs. Our dependence upon third parties for the manufacture of both drug substance and finished drug products that remain unpartnered may adversely affect our ability to develop and deliver such products on a timely and competitive basis. Similarly, our dependence on our partners to arrange for their own supplies of finished drug products may adversely affect our revenues. If we, or our partners, are unable to engage or retain third party manufacturers on commercially acceptable terms, our products may not be commercialized as planned. Our strategy of relying on third parties for manufacturing capabilities presents the following risks:

- The manufacturing processes for most of our APIs have not been validated at the scale required for commercial sales;
- Delays in scale-up to commercial quantities and any change at the site of manufacture could delay clinical trials, regulatory submissions and ultimately the commercialization of our products;
- Manufacturers of our products are subject to the FDA's cGMP regulations, and similar foreign standards that apply, and we do not necessarily have full control over compliance with these regulations by third party manufacturers;
- If we need to change manufacturers, the FDA and comparable foreign regulators would require new testing and compliance inspections and the new manufacturers would have to be educated in the processes necessary for the production of our product candidates;
- Without satisfactory long-term agreements with manufacturers, we will not be able to develop or commercialize our product candidates as planned or at all;
- We may not have intellectual property rights, or may have to share intellectual property rights, to any improvements in the manufacturing processes or new manufacturing processes for our product candidates; and
- If we are unable to engage or retain an acceptable third party manufacturer for any of our product candidates, we would either have to develop our own manufacturing capabilities or delay the development of such product candidate.

We may not be successful in our efforts to expand our product portfolio.

A key element in our strategy is to develop and commercialize new ophthalmic and respiratory products. We are seeking to do so through our internal research program and through licensing or otherwise acquiring the rights to potential new drugs and drug targets.

A significant portion of the research that we are conducting involves new and unproven technologies. Research programs to identify new disease targets and product candidates require substantial technical, financial and human resources whether or not we ultimately identify any candidates. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- The research methodology used may not be successful in identifying potential product candidates; or
- Potential product candidates may on further study be shown to have harmful side effects or other characteristics that indicate they are unlikely to be successful drugs.

We may be unable to license or acquire suitable product candidates or products from third parties for a number of reasons. The licensing and acquisition of pharmaceutical products is a competitive area. A number of more established companies are also pursuing strategies to license or acquire products in our core therapeutic areas. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Other factors that may prevent us from licensing or otherwise acquiring suitable product candidates include the following:

- We may be unable to license or acquire the relevant technology on terms that would allow us to make an appropriate return on the product;
- Companies that perceive us to be their competitors may be unwilling to assign or license their product rights to us; or
- We may be unable to identify suitable products or product candidates within our area of expertise.

If we are unable to develop suitable potential product candidates through internal research programs or by obtaining rights to novel therapeutics from third parties, our business will suffer.

Our dependence on collaborative relationships may lead to delays in product development, lost revenues and disputes over rights to technology.

Our business strategy depends to some extent upon the formation of research collaborations, licensing and/or marketing arrangements. We currently have a development collaboration with Santen and development and commercialization collaborations with Allergan. The termination of any collaboration may lead to delays in product development and disputes over technology rights and may reduce our ability to enter into collaborations with other potential partners. Allergan and Santen may immediately terminate their agreements with us if we breach the applicable agreement and fail to cure the breach within sixty (60) days of being notified of such breach. If we materially breach our co-promotion agreement with Allergan for Elestat™, Allergan has the right to terminate the agreement upon ninety (90) days written notice if we fail to cure the breach within that ninety (90) day period. If we do not maintain the Allergan or Santen collaborations, or establish additional research and development collaborations or licensing arrangements, it will be difficult to develop and commercialize products using our technology. Any future collaborations or licensing arrangements may not be on terms favorable to us.

Our current or any future collaborations or licensing arrangements ultimately may not be successful. Under our current strategy, and for the foreseeable future, we do not expect to develop or market products on our own in all global markets. As a result, we will continue to depend on collaborators and contractors for the preclinical study and clinical development of therapeutic products and for manufacturing and marketing of products which result from our technology. Our agreements with collaborators typically allow them some discretion in electing

whether to pursue such activities. If any collaborator were to breach or terminate its agreement with us or otherwise fail to conduct collaborative activities in a timely and successful manner, the preclinical or clinical development or commercialization of product candidates or research programs would be delayed or terminated. Any delay or termination in clinical development or commercialization would delay or eliminate potential product revenues relating to our research programs.

Disputes may arise in the future over the ownership of rights to any technology developed with collaborators. These and other possible disagreements between us and our collaborators could lead to delays in the collaborative development or commercialization of therapeutic or diagnostic products. Such disagreement could also result in litigation or require arbitration to resolve.

We may not be able to successfully compete with other biotechnology companies and established pharmaceutical companies.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Our competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions. These competitors include Alcon, AstraZeneca, Aventis, Bristol-Myers Squibb, Boehringer Ingelheim, Chiron, Genentech, GlaxoSmithKline, The Medicines Company, MedPointe Pharmaceuticals, Millennium Pharmaceuticals, Novartis, Pfizer, Otsuka, Schering-Plough and Senju. Most of these competitors have greater financial and other resources than we or our collaborative partners, including larger research and development staffs and more experienced marketing and manufacturing organizations.

In addition, most of our competitors have greater experience than we do in conducting preclinical and clinical trials and obtaining FDA and other regulatory approvals. Accordingly, our competitors may succeed in obtaining FDA or other regulatory approvals for product candidates more rapidly than we do. Companies that complete clinical trials, obtain required regulatory approvals, and commence commercial sale of their drugs before we do may achieve a significant competitive advantage, including patent and FDA marketing exclusivity rights that would delay our ability to market products. Drugs resulting from our research and development efforts, or from our joint efforts with our collaborative partners, may not compete successfully with competitors' existing products or products under development.

Acquisitions of competing companies and potential competitors by large pharmaceutical companies or others could enhance financial, marketing and other resources available to such competitors. Academic and government institutions have become increasingly aware of the commercial value of their research findings and are more likely to enter into exclusive licensing agreements with commercial enterprises to market commercial products. Many of our competitors have far greater resources than we do and may be better able to afford larger license fees and milestones attractive to those institutions. Our competitors may also develop technologies and drugs that are safer, more effective, or less costly than any we are developing or which would render our technology and future drugs obsolete and non-competitive. Current products marketed to treat cystic fibrosis include Pulmozyme® and TOBI®. Current treatments for cardiovascular disease include Plavix®, an anti-platelet agent and Angiomax®, a thrombin inhibitor. Primary treatments for dry eye disease currently involve over-the-counter artificial tear replacement drops, punctal plugs and Restasis®. Elestat™ competes with other treatments for allergic conjunctivitis including antihistamines and mast cell stabilizers, such as Patanol®, Zaditor® and Optivar®. In addition, alternative approaches to treating diseases which we have targeted, such as gene therapy, may make our product candidates obsolete.

We will rely substantially on third parties to market, distribute and sell our products and those third parties may not perform.

We have developed a commercialization organization to co-promote Elestat™ and Restasis®, but we are dependent on Allergan, or other experienced third parties, to perform or assist us in the marketing, distribution or

sale of these products and our product candidates. In addition, we may not identify acceptable partners or enter into favorable agreements with them for our other product candidates. If third parties do not successfully carry out their contractual duties, meet expected sales goals, maximize the commercial potential of our products, we may be required to hire or expand our own staff and sales force to compete successfully, which may not be possible. If Allergan or other third parties do not perform, or assist us in performing, these functions, it could have an adverse effect on our operations.

We have had limited experience in sales, marketing or distribution of products.

We have established a sales force to market and distribute Elestat™, Restasis® as well as other potential products. Although the members of our sales force have had experience in sales with other companies, prior to 2004 we never had a sales force and we may undergo difficulties maintaining the sales force. We have incurred substantial expenses in establishing the sales force, including substantial additional expenses for the training and management of personnel, and the infrastructure to enable the sales force to be effective. We expect to continue to incur substantial expenses in the future. The costs of maintaining our sales force may exceed our product revenues. We compete with many companies that currently have extensive and well-funded marketing and sales operations. Many of these competing companies have had substantially more experience in, and financial resources for sales, marketing and distribution.

Failure to hire and retain key personnel or to identify, appoint and elect qualified directors, may hinder our product development programs and our business efforts.

We depend on the principal members of management and scientific staff, including Christy L. Shaffer, Ph.D., our Chief Executive Officer and a director, and Thomas R. Staab, II, our Chief Financial Officer and Treasurer. If these people leave us, we may have difficulty conducting our operations. We have not entered into agreements with any officers or any other members of our management and scientific staff that bind them to a specific period of employment. We also depend upon the skills and guidance of the independent members of our Board of Directors. In December 2004, one of our directors resigned to devote additional time to his consulting practice and other matters and in February 2005, our non-executive Chairman of the Board, W. Leigh Thompson, M.D., Ph.D., D.Sc., passed away. While our Board of Directors has instituted succession planning steps to identify qualified board candidates to fill open board seats, there can be no assurance that we can identify, appoint and elect qualified candidates to serve as new members of the Board of Directors. Our future success also will depend in part on our ability to attract, hire and retain additional personnel skilled or experienced in the pharmaceutical industry. There is intense competition for such qualified personnel. We may not be able to continue to attract and retain such personnel.

If our patent protection is inadequate, the development and any possible sales of our product candidates could suffer or competitors could force our products completely out of the market.

Our business and competitive position depends on our ability to continue to develop and protect our products and processes, proprietary methods and technology. Except for patent claims covering new chemical compounds, most of our patents are use patents containing claims covering methods of treating disorders and diseases by administering therapeutic chemical compounds. Use patents, while providing adequate protection for commercial efforts in the United States, may afford a lesser degree of protection in other countries due to their patent laws. Besides our use patents, we have patents and patent applications covering compositions (new chemical compounds), pharmaceutical formulations and processes for large-scale manufacturing. Many of the chemical compounds included in the claims of our use patents and process applications were known in the scientific community prior to our patent applications. None of our composition patents or patent applications cover these previously known chemical compounds, which are in the public domain. As a result, competitors may be able to commercialize products that use the same previously known chemical compounds used by us for the treatment of disorders and diseases not covered by our use patents. Such competitors' activities may reduce our revenues.

If we must defend a patent suit, or if we choose to initiate a suit to have a third party patent declared invalid, we may need to make considerable expenditures of money and management time in litigation. We believe that there is significant litigation in the pharmaceutical and biotechnology industry regarding patent and other intellectual property rights. A patent does not provide the patent holder with freedom to operate in a way that infringes the patent rights of others. While we are not aware of any patent that we are infringing, nor have we been accused of infringement by any other party, other companies may have, or may acquire, patent rights which we might be accused of infringing. A judgment against us in a patent infringement action could cause us to pay monetary damages, require us to obtain licenses, or prevent us from manufacturing or marketing the affected products. In addition, we may need to initiate litigation to enforce our proprietary rights against others. Should we choose to do this, as with the above, we may need to make considerable expenditures of money and management time in litigation. Further, we may have to participate in interference proceedings in the United States Patent and Trademark Office, or USPTO, to determine the priority of invention of any of our technologies.

Our ability to develop sufficient patent rights in our pharmaceutical, biopharmaceutical and biotechnology products to support commercialization efforts is uncertain and involves complex legal and factual questions. For instance, the USPTO examiners may not allow our claims in examining our patent applications. If we have to appeal a decision to the USPTO's Appeals Board for a final determination of patentability we could incur substantial legal fees.

Because we rely upon trade secrets and agreements to protect some of our intellectual property, there is a risk that unauthorized parties may obtain and use information that we regard as proprietary.

We rely upon the laws of trade secrets and non-disclosure agreements and other contractual arrangements to protect our proprietary compounds, methods, processes, formulations and other information for which we are not seeking patent protection. We have taken security measures to protect our proprietary technologies, processes, information systems and data, and we continue to explore ways to further enhance security. However, despite these efforts to protect our proprietary rights, unauthorized parties may obtain and use information that we regard as proprietary. Employees, academic collaborators and consultants with whom we have entered confidentiality and/or non-disclosure agreements may improperly disclose our proprietary information. In addition, competitors may, through a variety of proper means, independently develop substantially the equivalent of our proprietary information and technologies, gain access to our trade secrets, or properly design around any of our patented technologies.

If physicians and patients do not accept our product candidates, they will not be commercially successful.

Even if regulatory authorities approve our product candidates, those products may not be commercially successful. Acceptance of and demand for our products will depend largely on the following:

- Acceptance by physicians and patients of our products as safe and effective therapies;
- Reimbursement of drug and treatment costs by third party payors;
- Marketing and sales activities of competitors;
- Safety, effectiveness and pricing of alternative products; and
- Prevalence and severity of side effects associated with our products.

In addition, to achieve broad market acceptance of our product candidates, in many cases we will need to develop, alone or with others, convenient methods for administering the products. We intend that diquafosol for the treatment of dry eye disease will be applied from a vial containing a single day's dosage of non-preserved medication. Patients may prefer to purchase preserved medication for multiple doses. We have not yet established a plan to develop a multi-dose formulation. Although our partner, Santen, is developing a multi-dose formulation for use in their licensed territories, a multi-dose formulation has not been developed by our other

partner, Allergan, for use in the remainder of the world. INS37217 Ophthalmic is administered through an intravitreal injection. It may be beneficial to patients to have a sustained delivery device. We have not yet established a plan for a sustained delivery device for certain indications such as for chronic use. Similar challenges exist in identifying and perfecting convenient methods of administration for our other product candidates.

Our operations involve a risk of injury from hazardous materials, which could be very expensive to us.

Our research and development activities involve the controlled use of hazardous materials and chemicals. We cannot completely eliminate the risk of accidental contamination or injury from these materials. If such an accident were to occur, we could be held liable for any damages that result and any such liability could exceed our resources. In addition, we are subject to laws and regulations governing the use, storage, handling and disposal of these materials and waste products. The costs of compliance with these laws and regulations are substantial.

Our commercial insurance and umbrella policies include limited coverage designated for pollutant clean-up and removal and limited general liability coverage per occurrence and in the aggregate. The cost of these policies is significant and there can be no assurance that we will be able to maintain these policies or that coverage amounts will be sufficient to insure potential losses.

Use of our products may result in product liability claims for which we may not have adequate insurance coverage.

Clinical trials or manufacturing, marketing and sale of our potential products may expose us to liability claims from the use of those products. Although we carry clinical trial liability insurance and product liability insurance, we, or our collaborators, may not maintain sufficient insurance. If our insurance is insufficient, we do not have the financial resources to self-insure and it is unlikely that we will have these financial resources in the foreseeable future. If we are unable to protect against potential product liability claims adequately, we may find it difficult or impossible to continue to co-promote our products, or to commercialize the products we develop. If claims or losses exceed our liability insurance coverage, we may go out of business.

Insurance coverage is increasingly more difficult to obtain or maintain.

While we currently have insurance for our business, property, directors and officers, and our products; insurance is increasingly more costly and narrower in scope, and we may be required to assume more risk in the future. If we are subject to claims or suffer a loss or damage in excess of our insurance coverage, we may be required to share that risk in excess of our insurance limits. Furthermore, any claims made on our insurance policy may impact our ability to obtain or maintain insurance coverage at reasonable costs or at all in the future.

Future sales by stockholders into the public market may cause our stock price to decline.

Future sales of our common stock by current stockholders into the public market could cause the market price of our stock to fall. As of January 31, 2005, there were 41,861,280 shares of common stock outstanding. Of these outstanding shares of common stock, approximately 21,500,000 shares were sold in public offerings and are freely tradable without restriction under the Securities Act, unless purchased by our affiliates. In addition, we have the ability to issue additional shares of common stock under an active shelf registration statement, which we filed with the Securities and Exchange Commission on April 16, 2004. Up to 7,178,571 shares of our common stock are issued or issuable upon exercise of stock options that have been, or may be, issued pursuant to our stock plan. The shares underlying existing, and possible future stock awards have been registered pursuant to a registration statement on Form S-8. The remaining shares of common stock outstanding are not registered under the Securities Act and may be resold in the public market only if registered or if there is an exemption from registration, such as Rule 144.

If some or all of such shares are sold into the public market over a short period of time, the value of all publicly traded shares is likely to decline, as the market may not be able to absorb those shares at then-current market prices. Such sales may make it more difficult for us to sell equity securities or equity-related securities in the future at a time and price that our management deems acceptable, or at all.

Further, we may issue additional shares:

- To employees, directors and consultants;
- In connection with corporate alliances;
- In connection with acquisitions; and
- To raise capital.

As of January 31, 2005, there were outstanding options, which were exercisable to purchase 2,592,544 shares of our common stock, and outstanding warrants, which were exercisable to purchase 25,396 shares of our common stock. This amount combined with the total common stock outstanding at January 31, 2005 is 44,479,220 shares of common stock.

As a result of these factors, a substantial number of shares of our common stock could be sold in the public market at any time.

Our rights agreement, the provisions of our Change in Control Severance Benefit Plan and our Change in Control Agreements with management, the anti-takeover provisions in our amended and restated certificate of incorporation and bylaws, and our right to issue preferred stock, may discourage a third party from making a take-over offer that could be beneficial to us and our stockholders and may make it difficult for stockholders to replace the board of directors and effect a change in our management if they desire to do so.

In October 2002, we entered into a Rights Agreement with Computershare Trust Company. The Rights Agreement could discourage, delay or prevent a person or group from acquiring 15% or more of our common stock. The Rights Agreement provides that if a person acquires 15% or more of our common stock without the approval of our board of directors, all other stockholders will have the right to purchase securities from us at a price that is less than its fair market value, which would substantially reduce the value of our common stock owned by the acquiring person. As a result, our board of directors has significant discretion to approve or disapprove a person's efforts to acquire 15% or more of our common stock.

Effective as of January 28, 2005, the Compensation Committee of the Board of Directors of Inspire adopted the Company's Change in Control Severance Benefit Plan, or the CIC Plan, which provides severance benefits to certain employees of the Company as of the date on which a Change in Control occurs. Under the CIC Plan and the change in control agreements discussed below, a Change in Control occurs upon a determination by the Board of Directors or upon certain specified events such as merger and consolidation. The CIC Plan covers any regular full-time or part-time employee, other than employees who are parties to employment agreements or transition agreements or who are parties to any severance plan or agreement with the Company (other than the CIC Plan) that provides for the payment of severance benefits in connection with a Change in Control. Under the CIC Plan, if a Change in Control occurs and a participant's employment is involuntarily terminated within two years, the participant will be entitled to certain payments and benefits based on the participant's salary range and years of service with the Company. Presently, all executive officers of the Company are parties to individual agreements with the Company regarding a Change in Control or, in one case, a transition agreement and, as a result, are not covered by the CIC Plan. On January 31, 2005, the Company and various executive officers entered into amended and restated change in control agreements. Each agreement is effective as of the date of the prior agreement between the Company and the respective executive officer. Each agreement provides that upon the officer's termination of employment following a Change in Control, unless such termination is for "cause,"

because of death or disability or by the officer without "good reason," within twenty-four (24) months following such Change in Control, the executive will be entitled to a lump sum payment equal to a multiple of the sum of (i) the highest annual base salary received by the officer in any of the three (3) most recently completed fiscal years prior to the Change in Control and (ii) the higher of the highest annual bonus received by the officer in any of the three (3) most recently completed fiscal years preceding the date of the officer's termination, the three (3) most recent completed fiscal years preceding the Change in Control, or the maximum of the bonus opportunity range for the officer immediately prior to the date of termination. The multiples used to determine the amount of a lump sum payment range from two (2) to three (3). The agreements also provide for ongoing benefits, the vesting of outstanding stock options, and gross-up payments. The CIC Plan and the change in control agreements would increase the acquisition costs to a purchasing company that triggers the change in control provisions. As a result, the CIC Plan and the change in control agreements may delay or prevent a change in control.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions which could delay or prevent a third party from acquiring shares of our common stock or replacing members of our board of directors. Our amended and restated certificate of incorporation allows our board of directors to issue shares of preferred stock. The board can determine the price, rights, preferences and privileges of those shares without any further vote or action by the stockholders. As a result, our board of directors could make it difficult for a third party to acquire a majority of our outstanding voting stock. Since management is appointed by the board of directors, any inability to effect a change in the board may result in the entrenchment of management.

Our amended and restated certificate of incorporation also provides that the members of the board will be divided into three classes. Each year the terms of approximately one-third of the directors will expire. Our amended and restated bylaws do not permit our stockholders to call a special meeting of stockholders. Under the bylaws, only our Chief Executive Officer, President, Chairman of the Board, Vice-Chairman of the Board or a majority of the board of directors are able to call special meetings. The staggering of directors' terms of office and the inability of stockholders to call a special meeting may make it difficult for stockholders to remove or replace the board of directors should they desire to do so. The bylaws also require that stockholders give advance notice to our Secretary of any nominations for director or other business to be brought by stockholders at any stockholders' meeting. These provisions may delay or prevent changes of control or management, either by third parties or by stockholders seeking to change control or management.

We are also subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. Under these provisions, if anyone becomes an "interested stockholder," we may not enter a "business combination" with that person for three years without special approval, which could discourage a third party from making a take-over offer and could delay or prevent a change of control. For purposes of Section 203, "interested stockholder" means, generally, someone owning 15% or more of our outstanding voting stock or an affiliate of ours that owned 15% or more of our outstanding voting stock during the past three years, subject to certain exceptions as described in Section 203.

FORWARD LOOKING INFORMATION

This annual report on Form 10-K, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, that are subject to the "safe harbor" created by those sections. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as "anticipate," "estimate," "plan," "project," "continuing," "believe," "expect," "future" and "intend" and similar expressions to identify forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated by any forward-looking statements, including, without limitation, the risk factors

listed above and those relating to product development, revenue and earnings expectations, intellectual property rights and litigation, competitive products, results of clinical trials, the need for additional research and testing, delays in manufacturing, funding and the timing and content of decisions made by regulatory authorities, including the FDA and other factors presented throughout this annual report and any other documents filed by us with the Securities and Exchange Commission.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this annual report on Form 10-K or in any document incorporated by reference might not occur. Stockholders are cautioned not to place undue reliance on the forward-looking statements, which speak only of the date of this report or the date of the document incorporated by reference in this document. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

Item 2. Properties.

We lease contiguous administrative and laboratory facilities that comprise approximately 51,000 square feet in Durham, North Carolina, which is adjacent to the Research Triangle Park. The various leases underlying our facilities expire in November 2006 and are renewable. We believe our facilities will be adequate to meet our operational needs through November 2006 when our leases expire.

Item 3. Legal Proceedings.

On February 15, 2005, a purported class action complaint was filed in the United States District Court for the Middle District of North Carolina by Mirco Investors, LLC on behalf of itself and all other similarly situated investors against us and certain of our senior officers. The complaint alleges violations of sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Securities and Exchange Commission Rule 10b-5, and focuses on statements that are claimed to be false and misleading regarding a Phase 3 clinical trial of our dry eye product candidate, diquafosol. The plaintiffs seek unspecified damages on behalf of a purported class of purchasers of our securities during the period from June 2, 2004 through February 8, 2005. On February 16, 2005, a similar complaint against the same defendants was filed by Richard and Susan Giorgino. In addition, on March 4, 2005, a similar complaint against the same defendants was filed by Kiah Sai Tan. It is possible that additional complaints may be filed in the future. We expect that these individual lawsuits will be consolidated into a single civil action. We intend to defend the litigation vigorously.

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

Not applicable.

PART II

Item 5. Market for the Company's Common Equity, Related Stockholder Matters and Issuer Purchase of Equity Securities.

Our common stock has been traded on the Nasdaq National Market under the symbol "ISPH" since August 3, 2000. The following table sets forth, for the calendar periods indicated, the range of high and low sale prices for our common stock on the Nasdaq National Market:

2003	High	Low
First Quarter	$15.89	$ 9.06
Second Quarter	$16.35	$10.53
Third Quarter	$18.77	$10.10
Fourth Quarter	$21.37	$12.37

2004	High	Low
First Quarter	$15.42	$10.76
Second Quarter	$18.74	$12.60
Third Quarter	$17.04	$11.37
Fourth Quarter	$19.19	$14.75

As of January 31, 2005, there were 61 record stockholders and over 8,000 beneficial stockholders of our common stock. On January 31, 2005, the last sale price reported on the Nasdaq National Market for our common stock was $14.80 per share.

We have not paid or declared dividends on our common stock since our inception and do not plan to pay dividends on our common stock in the foreseeable future. Any earnings that we may realize will be retained to finance our growth.

On November 19, 2004, we issued 5,728 shares of common stock to a consultant upon the exercise of warrants at a price of $4.20 per share. On December 17, 2004, we issued 253,968 shares of common stock to Genentech, Inc. upon the exercise of warrants at a price of $7.88 per share. The issuance of these shares was deemed to be exempt from registration under the Securities Act by virtue of Section 4(2) as a transaction not involving any public offering. The transferees made appropriate representations as part of the settlements and had, or had access to, adequate information about Inspire. An appropriate legend was affixed to the stock certificates that were issued.

Item 6. Selected Financial Data.

The selected statement of operations data and balance sheet data with respect to the years ended December 31, 2004, 2003, 2002, 2001 and 2000 set forth below are derived from our financial statements. The selected financial data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in Item 7 below, and our financial statements and the notes thereto appended to this annual report. Historical results are not necessarily indicative of our future results.

	(in thousands, except per share amounts)				
	Year Ended December 31,				
	2004	2003	2002	2001	2000
Statement of Operations Data:					
Revenue	$ 11,068	$ 5,200	$ 4,883	$ 7,285	$ 5,368
Operating expenses:					
Research and development	25,698	27,631	25,229	28,193	16,354
Selling and marketing	21,848	2,838	60	124	—
General and administrative	9,041	7,002	5,091	5,758	3,730
Total operating expenses	56,587	37,471	30,380	34,075	20,084
Loss from operations	(45,519)	(32,271)	(25,497)	(26,790)	(14,716)
Other income, net	1,450	876	804	3,655	1,126
Loss before provision for income taxes	(44,069)	(31,395)	(24,693)	(23,135)	(13,590)
Provision for income taxes	—	—	—	—	400
Net loss	(44,069)	(31,395)	(24,693)	(23,135)	(13,990)
Preferred stock dividends	—	—	—	—	(594)
Net loss available to common stockholders	$(44,069)	$(31,395)	$(24,693)	$(23,135)	$(14,584)
Net loss per common share—basic and diluted	$ (1.25)	$ (1.03)	$ (0.96)	$ (0.90)	$ (1.23)
Common shares used in computing weighted average common shares outstanding—basic and diluted	35,261	30,526	25,821	25,702	11,871

	(in thousands)				
	December 31,				
	2004	2003	2002	2001	2000
Balance Sheet Data:					
Cash and cash equivalents	$ 100,320	$ 34,324	$ 27,128	$ 29,959	$ 35,109
Investments	56,476	40,842	4,501	27,895	44,026
Total assets	165,696	79,678	33,564	60,087	82,993
Capital lease obligations, including current portion	1,881	1,084	505	901	812
Deferred revenue	—	—	2,200	4,083	6,368
Common stock	42	32	26	26	26
Accumulated deficit	(171,163)	(127,094)	(95,699)	(71,006)	(47,871)
Total stockholders' equity	149,598	71,052	28,998	52,595	74,505

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

Cautionary Statement

The discussion below contains forward-looking statements regarding our financial condition and our results of operations that are based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted within the United States, as well as projections for the future. The preparation of these financial statements requires our management to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. We evaluate our estimates on an ongoing basis. These estimates are based on historical experience and on various other assumptions that are believed to be reasonable under the circumstances. The results of these estimates form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources.

We operate in a highly competitive environment that involves a number of risks, some of which are beyond our control. We are subject to risks common to biopharmaceutical companies, including risks inherent in our research, development and commercialization efforts, preclinical testing, clinical trials, uncertainty of regulatory and marketing approvals, reliance on collaborative partners, enforcement of patent and proprietary rights, the need for future capital, potential competition associated with our product candidates, use of hazardous materials and retention of key employees. In order for one of our product candidates to be commercialized, it will be necessary for us to conduct preclinical tests and clinical trials, demonstrate efficacy and safety of the product candidate to the satisfaction of regulatory authorities, obtain marketing approval, enter into manufacturing, distribution and marketing arrangements, obtain market acceptance and, in many cases, obtain adequate reimbursement from government and private insurers. We cannot provide assurance that we will generate significant revenues or achieve and sustain profitability in the future. Statements contained in Management's Discussion and Analysis of Financial Conditions and Results of Operations which are not historical facts are, or may constitute, forward-looking statements. Forward-looking statements involve known and unknown risks that could cause our actual results to differ materially from expected results. These risks are discussed in the section entitled "Risk Factors." Although we believe the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

Our operating expenses are difficult to predict and will depend on several factors. Development expenses, including expenses for drug synthesis and manufacturing, preclinical testing and clinical research activities, will depend on the ongoing requirements of our drug development programs, availability of capital and direction from regulatory agencies, which are difficult to predict. Management may in some cases be able to control the timing of development expenses in part by accelerating or decelerating preclinical testing, other discovery and basic research activities and clinical trial activities, but many of these expenditures will occur irrespective of whether our product candidates are approved when anticipated or at all. We have begun to incur significant selling and marketing expenses to successfully commercialize our products. Once again, management may in some cases be able to control the timing of these expenses, but many of these expenditures will occur irrespective of the commercial success of our products, at least initially. As a result of these factors, we believe that period to period comparisons are not necessarily meaningful and you should not rely on them as an indication of future performance. Due to all of the foregoing factors, it is possible that our consolidated operating results will be below the expectations of market analysts and investors. In such event, the prevailing market price of our common stock could be materially adversely affected.

Overview

We are a biopharmaceutical company dedicated to discovering, developing and commercializing prescription pharmaceutical products in disease areas with significant commercial markets and unmet medical needs. We were incorporated in October 1993 and commenced operations in March 1995 following our first substantial financing and licensing of the initial technology from UNC. We are located in Durham, North Carolina, adjacent to the Research Triangle Park.

Our goal is to build and commercialize a sustainable pipeline of innovative new treatments based upon our technical and scientific expertise, focusing in the ophthalmic and respiratory therapeutic areas. Our ophthalmic

products and clinical product candidates are currently concentrated in the allergic conjunctivitis, dry eye disease, corneal wound healing and retinal disease indications. In addition, we also have a preclinical program to treat glaucoma. We are also working on a product candidate for the treatment of respiratory complications of cystic fibrosis and an antiplatelet product candidate that could be utilized in cardiopulmonary bypass procedures.

We have several product candidates in various stages of clinical development and various programs in preclinical development. All of our clinical product candidates are based on proprietary technology relating to P2 receptors. Our most clinically advanced product candidates are $P2Y_2$ receptor agonists that target ophthalmology and respiratory conditions and diseases where current treatments are not adequate.

We have acquired the rights to market Elestat™ and Restasis® in the United States under co-promotion agreements with Allergan, and we receive co-promotion revenue based upon net sales of these products. In January 2004, we completed the hiring and training of our specialty sales force, at which time we began co-promoting Restasis® for dry eye disease. In February 2004, we launched Elestat™ for the treatment of allergic conjunctivitis.

In the first quarter of 2004, we emerged out of the development stage, having transformed into a commercial organization, and began receiving co-promotion revenue from the commercial product sales of Elestat™ and Restasis®. Previously, we devoted substantially all of our efforts to the discovery and clinical development of our product candidates as well as the establishment of strategic partnerships. Prior to 2004, our revenues consisted of payments under our various corporate partnerships established for the development and commercialization of our products when approved.

We have incurred significant operating losses since our inception and, as of December 31, 2004, we had an accumulated deficit of $171.2 million. We expect to incur losses for the next several years. We have financed our operations through proceeds received from the sale of equity securities including private sales of preferred stock and public offerings of common stock, as well as revenues received under corporate collaborations and the co-promotion of Elestat™ and Restasis®. We operate in a single business segment and do not have any foreign operations.

On June 27, 2003, we submitted an NDA to the FDA for our dry eye product candidate, and we were notified that our NDA was granted a "priority review" on July 31, 2003. On December 19, 2003, we received an approvable letter from the FDA. Since the initial submission of the NDA, we have completed two additional diquafosol Phase 3 clinical trials, trials 108 and 109. Although neither of the two additional diquafosol Phase 3 clinical trials met their primary endpoint, we plan to submit an amendment to our diquafosol NDA by June 30, 2005 based upon the totality of data from our diquafosol clinical program, including positive data on certain secondary endpoints and analyses from the 108 and 109 clinical trials. We intend to consult with Allergan to determine a European regulatory filing strategy for diquafosol for the treatment of dry eye disease.

In December 2003, we entered into an agreement with Allergan to co-promote Elestat™ in the United States. Allergan records all product sales and retains all product costs and licensing rights, with the exception of primary selling, promotional and marketing activities in the United States which is our responsibility. Under the terms of the agreement, we paid Allergan an up-front payment and Allergan pays co-promotion revenue to us on U.S. net sales of Elestat™. In February 2004, we began to receive co-promotion revenue from Allergan on net sales of Elestat™ upon our launch and co-promotion of Elestat™ in the United States.

In June 2001, we entered into a joint license, development and marketing agreement with Allergan to develop and commercialize diquafosol and granted the right to co-promote Restasis® in the United States. Under the terms of this agreement, we have received up-front and milestone payments of $11 million and may receive up to an additional $28 million in milestone payments assuming the successful completion of all remaining milestones under this agreement. In the third quarter of 2003, we exercised our right to co-promote Restasis® and diquafosol and we began co-promotion activities of Restasis® in January 2004. Allergan records all product sales and retains all product costs and licensing rights with the exception of costs for our domestic sales force which is our responsibility. We receive co-promotion revenue based upon net sales of Restasis® and we will receive diquafosol

co-promotion revenue for worldwide, except Asia, net sales if and when the product candidate is approved by regulatory agencies. We began receiving co-promotion revenue on net sales of Restasis® in April 2004.

In October 2002, we entered into a study funding agreement with the CFFT pursuant to which they funded the majority of the external costs of one Phase 2 trial for the treatment of cystic fibrosis in exchange for a milestone payment upon FDA approval, and the possibility of a sales milestone upon the commercialization and the achievement of a certain aggregate sales volume in the first five years following product approval. In the event of FDA approval, we are obligated to pay to the CFFT, over a period of five years, an amount equal to a multiple of the clinical trial costs incurred by the CFFT as a development milestone payment, which is currently estimated to be approximately $12 million. Additionally, in the event aggregate sales of the product exceed a certain level in the first five years subsequent to regulatory approval, we are obligated to pay the CFFT an additional $4 million sales milestone, payable over two years.

In December 1998, we entered into a Development, License and Supply Agreement with Santen for the development of diquafosol for the therapeutic treatment of ocular surface diseases. We are obligated to supply Santen with its requirements of diquafosol in bulk drug substance form for all preclinical studies, clinical trials and commercial requirements at agreed-upon prices. Under the agreement, we received an up-front equity investment of $1.5 million for shares of our stock and a milestone payment of $500,000. In addition, if all milestones are met, we could receive additional payments of up to $4.25 million, as well as royalties on net sales of licensed products. Santen is developing diquafosol in Japan and nine other Asian countries, and is currently in Phase 2 clinical trials.

Critical Accounting Policies and Estimates

Our financial statements, which have been prepared in accordance with generally accepted accounting principles, require us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosure of contingent assets and liabilities. We evaluate our estimates, judgments and the policies underlying these estimates on a periodic basis as situations change, and regularly discuss financial events, policies, and issues with members of our audit committee and our independent auditors. In addition, recognition of revenue from product co-promotion is affected by certain estimates and judgments made by Allergan on which we rely in recording this revenue on a quarterly basis. We routinely evaluate our estimates and policies regarding revenue recognition, taxes, clinical trial, preclinical/toxicology and manufacturing liabilities.

Revenue Recognition

We recognize revenue from product co-promotion based on net sales for Elestat™ and Restasis®, as defined in the co-promotion agreements, and as reported to us by our collaborative partner, Allergan. Accordingly, our co-promotion revenue is based upon Allergan's revenue recognition policy, other accounting policies and the underlying terms of our co-promotion agreements. Allergan recognizes revenue from product sales when goods are shipped and title and risk of loss transfers to the customer. The co-promotion agreements provide for gross sales to be reduced by estimates of sales returns, credits and allowances, normal trade and cash discounts, managed care sales rebates and other allocated costs as defined in the agreements. We also reduce gross sales for incentive programs we manage, estimating the proportion of sales that are subject to such incentive programs and reducing revenue appropriately. Under the Elestat™ co-promotion agreement, we are obligated to meet predetermined minimum annual net sales performance levels. If the annual minimum is not satisfied, we record a reduced percentage of net sales based upon our level of achievement of predetermined calendar year net sales target levels. Amounts contractually due from Allergan in excess of recorded co-promotion revenue are recorded as deferred revenue.

We recognize milestone revenue under our collaborative research and development agreements when we have performed services under such agreements or when we or our collaborative partner has met a contractual milestone triggering a payment to us. Non-refundable fees received at the initiation of collaborative agreements for which we have an ongoing research and development commitment are deferred and recognized ratably over the period of ongoing research and clinical development commitment. We are also entitled to receive milestone

payments under our collaborative research and development agreements based upon achievement of development milestones by us or our collaborative partners. We recognize milestone payments as revenues ratably over the period of our research and development commitment. The recognition period begins at the date the milestone is achieved and acknowledged by the collaborative partner, which is generally at the date payment is received from the collaborative partner, and ends on the date that we have fulfilled our research and development commitment. This period is based on estimates by management and the progress towards milestones in our collaborative agreements. The estimate is subject to revision as our development efforts progress and we gain knowledge regarding required additional development. Revisions in the commitment period are made in the period that the facts related to the change first become known. This may cause our revenue to fluctuate from period to period.

Taxes

Significant management judgment is required in determining our provision for income taxes, deferred tax assets and liabilities and any valuation allowance recorded against net deferred tax assets. We have recorded a valuation allowance of $74.9 million as of December 31, 2004 against all potential tax assets due to uncertainties related to our ability to utilize deferred tax assets, primarily consisting of certain net operating losses carried forward, before they expire. The valuation allowance is based on estimates of taxable income in each of the jurisdictions in which we operate and the period over which our deferred tax assets will be recoverable.

Liabilities

We generally enter into contractual agreements with third party vendors to provide clinical, preclinical/ toxicology, manufacturing, research and other services in the ordinary course of business. Many of these contracts are subject to milestone-based invoicing and the contract could be conducted over an extended period of time. We record liabilities under these contractual commitments when we determine an obligation has been incurred, regardless of the timing of the invoice. We monitor all significant research and development, manufacturing, promotion and marketing and other service activities and the related progression of work for these activities. We estimate the underlying obligation for each activity based upon our estimate of the amount of work performed and compare the estimated obligation against the amount that has been invoiced. Because of the nature of contracts and related delay in the contract's invoicing, the obligation to these vendors may be based upon management's estimate of the underlying obligation. We record the larger of our estimated obligation or invoiced amounts for completed service. In all cases, actual results may differ from our estimate.

Stock Option Expense

See discussion of the adoption of Statement of Financial Accounting Standards, or SFAS, No. 123 (revised 2004), "*Share-Based Payment,*" a revision of Financial Accounting Standards Board No. 123, "*Accounting for Stock-Based Compensation.*"

Impact of Inflation

Although it is difficult to predict the impact of inflation on our costs and revenues in connection with our products, we do not anticipate that inflation will materially impact our costs of operation or the profitability of our products when marketed.

Results of Operations

Years Ended December 31, 2004, 2003 and 2002

Revenues

Our revenues for the year ended December 31, 2004 were $11.1 million, compared to $5.2 million in 2003 and $4.9 million in 2002. The change in revenue in 2004 as compared to 2003 relates to our recording co-promotion revenue from Elestat™ and Restasis® commercial product sales in 2004 as compared to

collaborative revenue associated with 2003 milestone payments and amortization of deferred revenue recognized in 2003 under our collaborative research and development agreements with strategic partners. The increase in 2003 revenues, as compared to 2002, relates primarily to our receipt of a milestone payment from our strategic partner, Allergan. Fluctuations in revenue between the periods relate to fluctuations in product sales and the associated co-promotion revenue we receive and the timing and magnitude of milestone payments and amortization of deferred revenue recognized under our collaborative agreements.

Revenue from product co-promotion relates to U.S. net sales of Elestat™ and Restasis® according to the terms of our collaborative agreements with Allergan. We began realizing co-promotion revenue from Elestat™ beginning in February 2004, upon its launch in the United States, and recorded $9.6 million of revenue from net sales of Elestat™ in the eleven-month period. Elestat™ continues to increase market share and to be widely accepted by patients and physicians, becoming the second most prescribed allergic conjunctivitis product in our target universe, the top 200 highest prescribing ophthalmologists, optometrists, and allergists in each of our 64 sales territories in the United States. Based upon weekly national prescription data from IMS Health for the week ending December 31, 2004, Elestat™ has achieved over 16% market share in new prescription volume and over 14% market share in total prescriptions in our target universe. In regards to the total United States allergic conjunctivitis market, Elestat™ represents approximately 8% of new prescriptions and approximately 7% of total prescriptions for the week ending December 31, 2004, based on data compiled and reported by IMS Health. Elestat™ is a seasonal product with product demand mirroring seasonal trends for topical allergic conjunctivitis products whereby there is usually a large increase in sales during the Spring and a lesser increase during the Summer and Fall.

In April 2004, we began receiving co-promotion revenue on Restasis®, the only FDA approved treatment for dry eye disease. Restasis® had significant growth in 2004, its first full year of commercial sales, contributing approximately $1.5 million to our 2004 co-promotion revenue. We anticipate that Restasis® will become a more significant component of our co-promotion revenue in 2005. Our entitled co-promotion percentage of net sales of Restasis® will increase in April 2005 and Allergan has forecasted net sales of Restasis® to be $140-160 million in 2005, as compared to $100 million in net sales in 2004.

Our future revenue will depend on the commercial success of Elestat™ and Restasis®, seasonality of sales of Elestat™, whether we enter additional collaboration or co-promotion agreements, achieve milestones under existing or future collaboration agreements and whether we obtain regulatory approvals.

Costs and Expenses

Research and Development Expenses

Research and development expenses for the year ended December 31, 2004 were $25.7 million, compared to $27.6 million in 2003 and $25.2 million in 2002. Research and development expenses vary according to the number of programs in preclinical and clinical development and the stage of development of our clinical programs. Later stage clinical programs tend to cost more than earlier stage programs due to the length of the trial and the number of patients enrolled in later stage clinical trials.

The decrease in 2004 expenses, as compared to 2003, relates to significantly decreased spending on INS37217 Intranasal and INS316 Diagnostic, which were partially offset by increased spending on key programs in aggressive clinical and preclinical development; including expenses associated with our 109 Phase 3 clinical trial of diquafosol, a Phase 2 clinical trial of INS37217 Respiratory, long-term toxicology studies of INS37217 Respiratory and a Phase 2 clinical trial of INS37217 Ophthalmic. In 2003, we reclassified the INS37217 Intranasal and INS316 Diagnostic programs to lower priority programs and correspondingly decreased the resources dedicated to them.

The increase in research and development expenses in 2003, as compared to 2002, was due to increased spending on our clinical programs, particularly our INS37217 Intranasal program, in which we completed a

Phase 3 clinical trial in perennial allergic rhinitis in 2003, and our INS37217 Ophthalmic program. Also in October 2002, we entered into a research and development agreement with the CFFT, whereby the expenses for one Phase 2 INS37217 Respiratory proof-of-concept clinical trial are funded by the CFFT, but we also record the corresponding expenses and liabilities as the CFFT incurs these costs. If we receive FDA approval for INS37217 Respiratory for the treatment of cystic fibrosis, we will be obligated to pay a development milestone, and possibly a sales milestone, to the CFFT. If we do not receive FDA approval, we will have no financial obligation to the CFFT, including the Phase 2 clinical trial costs the CFFT is funding on our behalf. As of December 31, 2004, we have recorded approximately $1.9 million of contingent liabilities associated with this agreement.

Research and development expenses include all direct costs, including salaries for our research and development personnel, consulting fees, clinical trial costs, sponsored research costs, clinical trial insurance, license fees and other fees and costs related to the development of product candidates.

Our research and development expenses for the years ended December 31, 2004, 2003 and 2002 and from the respective project's inception are shown below and includes the percentage of overall research and development expenditures for the years listed.

	(In thousands) Year ended December 31,						Cumulative from Inception (October 28, 1993) to December 31, 2004	
	2004	%	2003	%	2002	%		%
diquafosol tetrasodium (INS365 Ophthalmic)	$ 6,835	27	$ 5,896	21	$ 7,420	29	$ 35,746	24
INS37217 Respiratory (denufosol tetrasodium)	4,256	17	3,146	12	2,962	12	13,009	9
INS50589 Antiplatelet	3,211	12	2,751	10	170	1	6,444	4
INS37217 Ophthalmic (denufosol tetrasodium)	2,893	11	1,365	5	401	1	6,382	4
INS37217 Intranasal (denufosol tetrasodium)	480	2	6,723	24	4,471	18	12,639	9
INS316 Diagnostic (uridine 5'-triphosphate) [1]	746	3	2,873	10	2,423	10	8,823	6
Other discovery and development costs [2]	7,277	28	4,877	18	7,382	29	65,667	44
Total	$25,698	100	$27,631	100	$25,229	100	$148,710	100

(1) In September 2004, Kirin terminated its license for this drug candidate.

(2) Other discovery and development costs represent all unallocated research and development costs or those costs allocated to preclinical projects. These costs include personnel costs of our discovery programs, internal and external general research costs and other internal and external costs of other drug discovery and development programs.

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

Selling and Marketing Expenses

Selling and marketing expenses for the year ended December 31, 2004 were $21.8 million, compared to $2.8 million in 2003 and $60,000 in 2002. The increase in selling and marketing expenses in 2004, as compared to 2003, resulted from our first year of commercial operations, including increases in personnel, advertising and promotion expenses and other administrative costs to enable our active co-promotion of Restasis® and Elestat™.

The increase in selling and marketing expenses in 2003, as compared to 2002, resulted from increases in personnel and other administrative costs as we began building our sales and marketing infrastructure in the fourth quarter of 2003 for the co-promotion of Elestat™ and Restasis®.

Our selling and marketing expenses include all direct costs for our sales force and marketing programs. Our sales force expenses include training costs, salaries, fleet management and travel costs. Our marketing expenses include product management, promotion, advertising, public relations, Phase 4 clinical trial costs, physician training and continued medical education and other administrative expenses. We have one Phase 4 clinical trial for Elestat™ ongoing and are planning to initiate an additional Phase 4 clinical trial in 2005.

In December 2003, we began hiring 64 territory managers and 6 regional sales directors to provide us with national sales coverage for our ophthalmic products. Our commercial organization focuses its promotional efforts on approximately 8,500 highly prescribing ophthalmologists, optometrists and allergists in the United States. We began co-promoting Restasis® in January 2004 and launched Elestat™ in February 2004. Future selling and marketing expenses will depend on the level of our future commercialization activities. We expect selling and marketing expenses will increase in periods that immediately precede and follow product launches.

General and Administrative Expenses

General and administrative costs for the year ended December 31, 2004 were $9.0 million, compared to $7.0 million in 2003 and $5.1 million in 2002. Our general and administrative expenses consist primarily of personnel, facility and related costs for general corporate functions, including business development, finance, accounting, legal, human resources, quality/compliance, facilities and information systems. The increase in 2004 general and administrative expenses is primarily due to expenses necessary to support and maintain a commercial organization, costs associated with Sarbanes-Oxley compliance, as well as overall corporate growth. The increase in 2003 general and administrative expenses was primarily due to our increased development activities, building a sales and marketing infrastructure, and continuing corporate growth. Future general and administrative expenses will depend on the level of our future development and commercialization activities; however, we expect an increase in future professional fees as a result of recently filed litigation.

Other Income (Expense)

Other income, net totaled $1.5 million for the year ended December 31, 2004, compared to $0.9 million for 2003 and $0.8 million for 2002. Other income fluctuates from year to year based upon fluctuations in the interest income earned on variable cash and investment balances and realized gains and losses on investments offset by interest expense on debt obligations. The increase in 2004 other income, as compared to 2003, is primarily the result of a write-down of a strategic investment in 2003 and larger cash and investment balances as a result of stock offerings that generated net proceeds in excess of $119 million in 2004. The increase in 2003 other income, as compared to 2002, represents larger interest income earned on higher average cash and investment balances offset by interest expense and increased losses on our investments, including a write-down on a strategic investment. Future other income will depend on our future cash and investment balances, the return on these investments, as well as levels of debt and the associated interest rates.

Liquidity and Capital Resources

We have financed our operations through the sale of equity securities, including private sales of preferred stock and public offerings of common stock. We currently receive revenue from co-promotion of Elestat™ and Restasis®, but do not expect this revenue to exceed our 2005 operating expenses.

At December 31, 2004, we had net working capital of $134.6 million, an increase of approximately $68.3 million from $66.2 million at December 31, 2003. The increase in working capital is principally due to our successful offerings of common stock in July and November 2004, offset by the use of funds for our normal

operating expenses. In July 2004, we completed a public offering of 6.9 million shares of common stock, which included the full exercise of the underwriters' over-allotment option, at $12.00 per share. The net proceeds, after underwriting discounts and costs in connection with the sale and distribution of the securities, were approximately $77.1 million. In November 2004, we completed an offering of approximately 2.5 million shares of common stock, which included the full exercise of the underwriter's over-allotment option, at $17.10 per share. The net proceeds, after underwriting discounts and costs in connection with the sale and distribution of the securities, were approximately $42.3 million. Our principal sources of liquidity at December 31, 2004 were $100.3 million in cash and cash equivalents and $55.8 million in investments which are considered "available-for-sale", reflecting a $81.6 million increase of cash, cash equivalents and investment balances over those at December 31, 2003.

Our working capital requirements may fluctuate in future periods depending on many factors, including: the efficiency of manufacturing processes developed on our behalf by third parties; the number, magnitude, scope and timing of our drug development programs, the costs related to the potential FDA approval of diquafosol and denufosol; the cost, timing and outcome of regulatory reviews and changes in regulatory requirements; the costs of obtaining patent protection for our product candidates; the timing and terms of business development activities; the rate of technological advances relevant to our operations; the timing, method and cost of the commercialization of our product candidates; the level of required administrative and legal support; the availability of capital to support product candidate development programs we pursue, the commercial potential of our products and product candidates, outcome of pending litigation; and the potential expansion of facility space. We are targeting 2005 operating expenses of $59-65 million. This range, however, does not consider the impact of any non-cash stock option expense as required under SFAS No. 123(R)(issued in 2004). We intend to continue to offer stock options to attract and retain qualified employees and Board of Directors and we will be required to expense this non-cash cost beginning in the third quarter of 2005. Based upon stock options currently outstanding and the valuation model and assumptions consistent with 2004 quarterly calculations, we project stock option expense to be approximately $5 million for the last half of 2005.

We believe our existing cash, cash equivalents and investments, will be adequate to satisfy our anticipated working capital requirements beyond 2006. In order for us to continue operations beyond 2006, we will need to: (1) obtain product candidate approvals, (2) in-license commercial products, (3) obtain additional co-promotion agreements, and/or (4) raise additional capital through equity or debt financings or from other sources. Accordingly, we have the ability to sell approximately $13.9 million worth of common stock under an active shelf registration statement, which we filed with the Securities and Exchange Commission on April 16, 2004. However, additional funding may not be available on favorable terms from any of these sources or at all. Our ability to achieve our operating expense target range is subject to several risks including unanticipated cost overruns, the need to expand the magnitude or scope of existing development programs, the need to change the number or timing of clinical trials, unanticipated regulatory requirements, costs to successfully commercialize our products and product candidates, commercial success of our products and product candidates, unanticipated professional fees or settlements associated with pending litigation and other factors described under the Risk Factors located elsewhere in this report.

As part of our drug development strategy, we outsource significant amounts of our preclinical and clinical programs and the manufacture of drug substance used in those programs. Accordingly, we have entered into contractual commitments or purchase arrangements with various clinical research organizations, manufacturers of active pharmaceutical ingredients and/or drug product as well as with others. The amount of our financial commitments under these arrangements totaled approximately $6.3 million at December 31, 2004. In addition, we have other contractual commitments outside of drug development under arrangements which totaled approximately $1.3 million at December 31, 2004. These amounts may vary dependent upon the results of underlying studies, the completion of studies and/or projects and certain other variable components that may yield a result that differs from management's estimate. Also, at December 31, 2004, we have future contractual commitments to pay $3.8 million of lease obligations for our administrative offices, laboratory facilities and equipment. Our existing license, collaboration and sponsored research agreements may require future cash

payments. In the aggregate, these agreements may require payments of up to $14.5 million assuming the achievement of all development milestones and up to $4.0 million assuming the achievement of all sales milestones. Amounts payable by us under these agreements are uncertain and are contingent on a number of factors, including the progress of our discovery and drug development programs, our ability to obtain regulatory approvals, and the commercial success of our approved products. Additionally, we are obligated to pay royalties on net sales, if any, of certain product candidates currently in our portfolio. Some of our license agreements require minimum annual license preservation fees under our existing license agreements ranging from $5,000 to $10,000. In addition, if we obtain licenses on additional product candidates in the future, or if our collaborative arrangements identify additional product candidates, our license obligations would increase.

Subject to the information and qualifications included in the above paragraph, as of December 31, 2004, our contractual and potential obligations are as follows:

	(In thousands) Payment due by Period				
Contractual and Potential Obligations	**Total**	**Less than 1 year**	**1-2 years**	**3-5 years**	**More than 5 years**
Capital Lease Obligations	$ 2,194	$ 636	$1,282	$ 276	$ —
Operating Lease Obligations	1,628	887	719	22	—
Purchase Obligations	7,578	7,578	—	—	—
Minimum Annual Payments	145	25	50	50	20
Development Milestone Obligations	14,450	50	250	12,000	2,150
Sales Milestone Obligations	4,000	—	—	—	4,000
Total	$29,995	$9,176	$2,301	$12,348	$6,170

Litigation

On February 15, 2005, a purported class action complaint was filed in the United States District Court for the Middle District of North Carolina by Mirco Investors, LLC on behalf of itself and all other similarly situated investors against us and certain of our senior officers. The complaint alleges violations of sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Securities and Exchange Commission Rule 10b-5, and focuses on statements that are claimed to be false and misleading regarding a Phase 3 clinical trial of our dry eye product candidate, diquafosol. The plaintiffs seek unspecified damages on behalf of a purported class of purchasers of our securities during the period from June 2, 2004 through February 8, 2005. On February 16, 2005, a similar complaint against the same defendants was filed by Richard and Susan Giorgino. In addition, on March 4, 2005, a similar complaint against the same defendants was filed by Kiah Sai Tan. It is possible that additional complaints may be filed in the future. We expect that these individual lawsuits will be consolidated into a single civil action. We intend to defend the litigation vigorously. As with any legal proceeding, we cannot predict with certainty the eventual outcome of these pending lawsuits. Furthermore, we will have to incur expenses in connection with these lawsuits, which may be substantial. In the event of an adverse outcome, our business, future results of operations, financial position and/or cash flows could be materially affected. Moreover, responding to and defending the pending litigation will result in a diversion of management's attention and resources and an increase in professional fees.

Impact of Recently Issued Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards, or SFAS, No. 123(R) (revised 2004, or SFAS No. 123(R)), "*Share-Based Payment,*" a revision of FASB Statement No. 123 "*Accounting for Stock-Based Compensation,*" or SFAS No. 123. SFAS No. 123(R) supersedes Accounting Principles Board Opinion No. 25, "*Accounting for Stock Issued to Employees,*" or APB No. 25, and amends SFAS No. 95, "*Statement of Cash Flows.*" SFAS No. 123(R) requires all share-based payments to employees, including grants of employee stock options, to be recognized in the

income statement based on their fair values for all periods that begin after June 15, 2005. Pro forma disclosure will no longer be an alternative. SFAS No. 123(R) permits public companies to adopt its requirements using one of two methods:

1. A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS No. 123(R) for all share-based payments granted after the effective date and (b) based on the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123(R) that remain unvested on the effective date; or

2. A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS No. 123 for purposes of pro forma disclosures either for (a) all prior periods presented or (b) prior interim periods of the year of adoption.

We intend to adopt SFAS No. 123(R) effective July 1, 2005. As permitted by SFAS No. 123, we currently account for share-based payments to employees using APB No. 25's intrinsic value method and, as such, generally recognize no compensation cost for employee stock options. Accordingly, the adoption of SFAS No. 123(R)'s fair value method will have a significant impact on our results of operations and our overall financial position. An estimate of the non-cash stock option expense for the last half of 2005, based upon the current number of stock options outstanding and calculated using assumptions and a valuation model consistent with 2004 quarterly filings, is approximately $5 million. However, actual expense may be materially different depending on the valuation model, assumptions and methodologies used in implementing SFAS No. 123(R), as well as the number of unvested stock options outstanding during 2005.

In March 2004, the FASB issued Emerging Issues Task Force, or EITF, Issue No. 03-13, or EITF 03-13, "Applying the Conditions in Paragraph 42 of FASB Statement No. 144, or FASB No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets,* in Determining Whether to Report Discontinued Operations." The FASB staff established a working group to assist in the development of a model for evaluating (a) which cash flows are to be considered in determining whether cash flows have been or will be eliminated and (b) what types of continuing involvement constitute significant continuing involvement. We have adopted FASB No. 144 and EITF 03-13, and they have not had a material impact on our financial position, results of operations or cash flows.

In March 2004, the FASB issued EITF Issue No. 03-1, or EITF 03-1, *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments"* which provided new guidance for assessing impairment losses on investments. Additionally, EITF 03-1 included new disclosure requirements for investments that are deemed to be other-than-temporarily-impaired. We have adopted the disclosure requirements of EITF 03-1. In September 2004, the FASB delayed the effective date of application guidance on impairment of securities included within EITF 03-01 and is currently reconsidering conclusions reached in EITF 03-1.

In December 2003, the FASB issued Interpretation No. 46R, or FIN 46R, "*Consolidation of Variable Interest Entities*," which replaces Interpretation No. 46. FIN 46R requires existing unconsolidated variable interest entities, or VIEs, to be consolidated by their primary beneficiaries if the entities do not effectively disperse risk among the parties involved. VIEs that effectively disperse risks will not be consolidated unless a single party holds an interest or combination of interest that effectively recombines risks that were previously dispersed. Application of FIN 46R is required in financial statements of public entities that have interest in VIEs or potential VIEs, commonly referred to as special-purpose entities, for periods after December 31, 2003. Application by public entities for all other types of entities is required in its financial statements for periods ending after March 31, 2004. We do not have interests in VIEs. FIN 46R did not have any impact on our financial position, results of operations or cash flows.

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

Interest Rate Sensitivity

We are subject to interest rate risk on our investment portfolio. We maintain an investment portfolio consisting primarily of United States government and government agency obligations, money market investments, municipal notes and bonds and asset or mortgage-backed securities. Our portfolio has a current average maturity of less than 12 months, using the stated maturity or reset maturity dates associated with individual maturities as the basis for the calculation.

Our exposure to market risk for changes in interest rates relates to the increase or decrease in the amount of interest income we can earn on our investment portfolio, changes in the market value of investments due to changes in interest rates, the increase or decrease in realized gains and losses on investments and the amount of interest expense we must pay with respect to various outstanding debt instruments. Our risk associated with fluctuating interest expense is limited to capital leases and other short-term debt obligations. Under our current policies, we do not use interest rate derivative instruments to manage exposure to interest rate changes. We ensure the safety and preservation of invested principal funds by limiting default risk, market risk and reinvestment risk. We reduce default risk by investing in investment grade securities. Our investment portfolio includes only marketable securities and instruments with active secondary or resale markets to help ensure portfolio liquidity and we have implemented guidelines limiting the duration of investments. A hypothetical 100 basis point drop in interest rates along the entire interest rate yield curve would not significantly affect the fair value of our interest sensitive financial instruments. At December 31, 2004, our portfolio of available-for-sale investments consisted of approximately $41.4 million of investments maturing within one year and approximately $14.3 million of investments maturing after one year but within 36 months. In addition, we have $0.5 million of our long-term investments that are held in a restricted account that collateralizes a letter of credit with a financial institution. Additionally, we generally have the ability to hold our fixed-income investments to maturity and therefore do not expect that our operating results, financial position or cash flows will be affected by a significant amount due to a sudden change in interest rates.

Strategic Investment Risk

In addition to our normal investment portfolio, we have a strategic investment in Parion Sciences, Inc. valued at $0.2 million. This investment represents unregistered preferred stock and is subject to higher investment risk than our normal investment portfolio due to the lack of an active resale market for the investment.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. A list of the financial statements filed herewith is found at "Index to Financial Statements" on page F-1.

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

Not applicable.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management is responsible for establishing and maintaining an adequate system of internal control over our financial reporting. The design, monitoring and revision of the system of internal accounting controls involves, among other items, management's judgments with respect to the relative cost and expected benefits of specific control measures. The effectiveness of the control system is supported by the selection, retention and training of qualified personnel and an organizational structure that provides an appropriate division of responsibility and formalized procedures. The system of internal accounting controls is periodically reviewed and modified in response to changing conditions. Internal audit consultants regularly monitor the adequacy and effectiveness of internal accounting controls. In addition to the system of internal accounting controls, management maintains corporate policy guidelines that help monitor proper overall business conduct, possible conflicts of interest, compliance with laws and confidentiality of proprietary information. Our Chief Executive Officer and Chief Financial Officer have reviewed and evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. Based on that evaluation, the Chief Executive Officer and Chief Financial Officer have concluded that our current disclosure controls and procedures are effective in timely providing them with material information relating to us which is required to be disclosed in the reports we file or submit under the Securities Exchange Act of 1934.

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of our internal control that occurred during our last fiscal quarter, which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting as defined in Rules 13a-15(f) and 15d-15(f) of the Securities Exchange Act of 1934, and for performing an assessment of the effectiveness of internal control over financial reporting as of December 31, 2004. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our system of internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this evaluation, management, including our principal executive officer and principal financial officer, concluded that our internal control over financial

reporting was effective as of December 31, 2004. Management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report included herein, which expresses unqualified opinions on management's assessment of the effectiveness of internal control over financial reporting and on the effectiveness of our internal control over financial reporting as of December 31, 2004.

Audit Committee Oversight

The Audit Committee of the Board of Directors, consisting solely of outside directors, appoints the independent auditors and receives and reviews the reports submitted by them. The Audit Committee meets several times during the year with management, the internal auditors and the independent auditors to discuss audit activities, internal controls and financial reporting matters. The internal auditors and the independent auditors have full and free access to the Audit Committee.

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information required by this item is incorporated by reference to the sections of our definitive proxy statement to be filed with the SEC pursuant to Regulation 14A in connection with the 2005 Annual Meeting (the "Proxy Statement") to be contained under the headings "Election of Directors", "Executive Officers who are not Nominees," and "Section 16(a) Beneficial Ownership Reporting Compliance."

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference to the sections of our Proxy Statement to be contained under the headings "Executive Compensation," "Compensation Committee Report." and "Relative Stock Performance."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated by reference to the section of our Proxy Statement to be contained under the heading "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

To the extent applicable, the information required by this item is incorporated by reference to the sections of our Proxy Statement to be contained under the headings "Executive Compensation."

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated by reference to the sections of our Proxy Statement to be contained the heading "Audit and Other fees" and related captions.

ITEM 15. EXHIBITS and FINANCIAL STATEMENTS SCHEDULES

(a) The following documents are included as part of this Annual Report on Form 10-K:

1. Financial Statements:

2. All schedules are omitted as the information required is inapplicable or the information is presented in the financial statements.

3. Exhibits:

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation. (Incorporated by reference to Exhibit 3.1 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation (Incorporated by reference to Exhibit 3.2 to the Company's Annual Report on Form 10-K filed March 26, 2002).
3.3	Certificate of Designations of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.3 to the Company's Annual Report on Form 10-K filed March 7, 2003).
3.4	Amended and Restated Bylaws, as adopted March 30, 2004. (Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on April 15, 2004).
4.1	Specimen Common Stock Certificate. (Incorporated by reference to Exhibit 4.1 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
4.2	Rights Agreement, dated as of October 21, 2002, between the Company and Computershare Trust Company, which includes the form of Certificate of Designation of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. as Exhibit "A", the form of Rights Certificate as Exhibit "B" and the Summary of Rights to Purchase Preferred Stock as Exhibit "C" (Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on October 22, 2002).
10.1†	Amended and Restated 1995 Stock Plan, as amended. (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004).
10.2†	Form of Incentive Stock Option. (Incorporated by reference to Exhibit 10.2 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.3†	Form of Non-statutory Stock Option. (Incorporated by reference to Exhibit 10.3 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.4*	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and The University of North Carolina at Chapel Hill, dated March 10, 1995. (Incorporated by reference to Exhibit 10.7 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).

Exhibit Number	Description
10.5	Lease between Inspire Pharmaceuticals, Inc. and Imperial Center, Limited Partnership regarding Royal Center I, Durham, North Carolina, dated as of May 17, 1995, as amended. (Incorporated by reference to Exhibit 10.8 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.6	Lease Agreement between Inspire Pharmaceuticals, Inc. and Petula Associates Ltd. regarding Royal Center II, Durham, North Carolina, dated as of December 30, 1997. (Incorporated by reference to Exhibit 10.10 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.7	Sublease Agreement between ICAgen, Inc. and Inspire Pharmaceuticals, Inc. regarding premises located at 4222 Emperor Boulevard, Suite 500, Durham, North Carolina, dated September 22, 1997 and extension of Sublease Agreement dated February 14, 2000. (Incorporated by reference to Exhibit 10.11 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.8*	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and The University of North Carolina at Chapel Hill, dated September 1, 1998. (Incorporated by reference to Exhibit 10.12 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.9*	Development, License and Supply Agreement between Inspire Pharmaceuticals, Inc. and Santen Pharmaceutical Co., Ltd., dated as of December 16, 1998. (Incorporated by reference to Exhibit 10.15 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.10	Registration Rights Agreement between Inspire Pharmaceuticals, Inc. and Santen Pharmaceutical Co., Ltd., dated as of December 16, 1998. (Incorporated by reference to Exhibit 10.16 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.11	Warrant Agreement between Inspire Pharmaceuticals, Inc. and Genentech, Inc., dated as of December 17, 1999. (Incorporated by reference to Exhibit 10.22 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.12	Amended and Restated Investors' Rights Agreement among Inspire Pharmaceuticals, Inc. and the holders of Series A, B, E and G Preferred Stock of the Company dated as of December 17, 1999. (Incorporated by reference to Exhibit 10.23 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.13†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Donald Kellerman dated February 3, 2000. (Incorporated by reference to Exhibit 10.24 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.14†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Gregory J. Mossinghoff dated February 4, 2000. (Incorporated by reference to Exhibit 10.25 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.15†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Benjamin R. Yerxa dated February 4, 2000. (Incorporated by reference to Exhibit 10.26 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).

Exhibit Number	Description
10.16†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Christy L. Shaffer dated February 10, 2000. (Incorporated by reference to Exhibit 10.28 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.17†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Richard M. Evans dated February 10, 2000. (Incorporated by reference to Exhibit 10.30 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.18†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Mary Bennett dated February 27, 2001. (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 15, 2001).
10.19†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Joseph Schachle dated April 3, 2001. (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 10, 2001).
10.20*	License, Development and Marketing Agreement between Inspire Pharmaceuticals, Inc. and Allergan, Inc., dated as of June 22, 2001. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 29, 2001).
10.21*	Study Funding Agreement, dated as of October 3, 2002, between Inspire Pharmaceuticals, Inc. and The Cystic Fibrosis Foundation Therapeutics, Inc. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 4, 2002).
10.22	First Amendment to Lease Agreement between Inspire Pharmaceuticals, Inc. and Royal Center Two IC, LLC for Royal Center Two, Durham, North Carolina, dated as of June 28, 2002. (Incorporated by reference to Exhibit 10.31 to the Company's Annual Report on Form 10-K filed March 7, 2003).
10.23	Third Amendment to Lease Agreement between Inspire Pharmaceuticals, Inc. and Royal Center One IC, LLC for Royal Center One, Durham, North Carolina, dated as of June 28, 2002. (Incorporated by reference to Exhibit 10.32 to the Company's Annual Report on Form 10-K filed March 7, 2003).
10.24	Underwriting Agreement by and between Inspire Pharmaceuticals, Inc. and Deutsche Bank Securities and U.S. Bancorp Piper Jaffray Inc. dated March 13, 2003. (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed on March 14, 2003).
10.25	Second Amendment To Lease between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC dated as of June 6, 2003. (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.26†	Form of Inspire Pharmaceuticals, Inc. Employee Stock Option Agreement. (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.27†	Form of Inspire Pharmaceuticals, Inc. Director Non-Statutory Stock Option Agreement. (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.28*	First Amendment to License, Development and Marketing Agreement, dated December 8, 2003, between Inspire Pharmaceuticals, Inc. and Allergan, Inc. and Allergan Sales, LLC and Allergan Pharmaceuticals Holdings (Ireland) Ltd. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 9, 2003).
10.29*	Elestat (Epinastine) Co-Promotion Agreement, entered into as of December 8, 2003, by and between Allergan Sales, LLC and Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 1, 2004).

Exhibit Number	Description
10.30†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Thomas R. Staab, II, dated May 16, 2003. (Incorporated by reference to Exhibit 10.35 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.31	Second Amendment to Sublease and Consent between ICAgen, Inc., Inspire Pharmaceuticals, Inc. and Imperial Center Partnership and Petula Associates, Ltd., dated August 13, 2003 (Incorporated by reference to Exhibit 10.36 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.32	Master Lease Agreement between GE Capital Fleet Services and Inspire Pharmaceuticals, Inc., dated as of November 18, 2003, and related documentation (Incorporated by reference to Exhibit 10.38 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.33	Master Security Agreement between General Electric Capital Corporation and Inspire Pharmaceuticals, Inc., dated as of November 12, 2003, and related documentation (Incorporated by reference to Exhibit 10.39 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.34	Underwriting Agreement by and among Inspire Pharmaceuticals, Inc. and Morgan Stanley & Co. Incorporated, Deutsche Bank Securities Inc., Piper Jaffray & Co. and SG Cowen & Co., LLC dated July 26, 2004 (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed July 27, 2004).
10.35†	Agreement between Inspire Pharmaceuticals, Inc. and Christy Shaffer, effective as of March 29, 2004, regarding change in control (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004).
10.36†	Form of Change in Control Agreement for other executive officers (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004).
10.37	Third Amendment to Lease, dated as of August 4, 2004, between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on August 12, 2004.)
10.38	Fourth Amendment to Lease, dated as of August 4, 2004, between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on August 12, 2004.)
10.39†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between the Company and R. Kim Brazzell, dated August 5, 2004 (Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed November 9, 2004).
10.40†	Amended and Restated Director Compensation Policy.
10.41†	Agreement between Inspire Pharmaceuticals, Inc. and Barry G. Pea, effective as of October 11, 2004, regarding change in control.
10.42†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Barry G. Pea, dated October 13, 2004.
10.43†	Transition Agreement between Inspire Pharmaceuticals, Inc. and Gregory J. Mossinghoff, dated October 28, 2004.
10.44**	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and the Wisconsin Alumni Research Foundation, effective November 2, 2004.
10.45	Underwriting Agreement, dated November 10, 2004, by and between Inspire Pharmaceuticals, Inc. and Deutsche Bank Securities Inc. (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed November 12, 2004).

Exhibit Number	Description
10.46†	Inspire Pharmaceuticals, Inc. Change in Control Severance Benefit Plan (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.47†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Christy L. Shaffer (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.48†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Mary B. Bennett (Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.49†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Richard M. Evans (Incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.50†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Donald J. Kellerman (Incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.51†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Joseph K. Schachle (Incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.52†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Thomas R. Staab, II (Incorporated by reference to Exhibit 10.7 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.53†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Benjamin R. Yerxa (Incorporated by reference to Exhibit 10.8 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.54†	Agreement regarding change in control, dated as of August 2, 2004, by and between Inspire Pharmaceuticals, Inc. and R. Kim Brazzell (Incorporated by reference to Exhibit 10.9 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.55†	Agreement regarding change in control, dated as of October 11, 2004, by and between Inspire Pharmaceuticals, Inc. and Barry G. Pea (Incorporated by reference to Exhibit 10.10 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.56†	Form of Inspire Pharmaceuticals, Inc. Employee Stock Option Agreement.
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

* Confidential treatment has been granted with respect to a portion of this Exhibit.

** Confidential treatment has been requested with respect to a portion of this Exhibit.

† Denotes a management contract or compensation plan or arrangement required to be filed as an exhibit pursuant to Item 15(c) of this Form 10-K.

SIGNATURES

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

Inspire Pharmaceuticals, Inc.

By: /s/ CHRISTY L. SHAFFER
Christy L. Shaffer
Chief Executive Officer and Director

Date: March 11, 2005

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

Signature	Title	Date
/s/ CHRISTY L. SHAFFER **Christy L. Shaffer**	Chief Executive Officer (principal executive officer) and Director	March 11, 2005
/s/ THOMAS R. STAAB, II **Thomas R. Staab, II**	Chief Financial Officer (principal financial officer and principal accounting officer)	March 11, 2005
/s/ KENNETH B. LEE, JR. **Kenneth B. Lee, Jr.**	Chairman of the Board of Directors	March 11, 2005
/s/ KIP A. FREY **Kip A. Frey**	Director	March 11, 2005
/s/ RICHARD S. KENT **Richard S. Kent**	Director	March 11, 2005
/s/ WILLIAM R. RINGO, JR. **William R. Ringo, Jr.**	Director	March 11, 2005

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INSPIRE PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders
of Inspire Pharmaceuticals, Inc.:

We have completed an integrated audit of Inspire Pharmaceuticals, Inc.'s 2004 financial statements and of its internal control over financial reporting as of December 31, 2004 and audits of its 2003 and 2002 financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Our opinions, based on our audits, are presented below.

Financial statements

In our opinion, the accompanying balance sheets and the related statements of operations, of stockholders' equity and of cash flows present fairly, in all material respects, the financial position of Inspire Pharmaceuticals, Inc. at December 31, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements 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 of financial statements includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

Internal control over financial reporting

Also, in our opinion, management's assessment, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A, that the Company maintained effective internal control over financial reporting as of December 31, 2004 based on criteria established in *Internal Control - Integrated Framework* issued by The Committee of Sponsoring Organizations of the Treadway Commission (COSO), is fairly stated, in all material respects, based on those criteria. Furthermore, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on criteria established in *Internal Control - Integrated Framework* issued by the 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 opinions on management's assessment and on the effectiveness of the Company's internal control over financial reporting based on our audit. We conducted our audit of internal control over financial reporting 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. An audit of internal control over financial reporting includes 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 consider necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting

includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
March 11, 2005

INSPIRE PHARMACEUTICALS, INC.

BALANCE SHEETS
(in thousands, except per share amounts)

	December 31, 2004	December 31, 2003
Assets		
Current assets:		
Cash and cash equivalents	$ 100,320	$ 34,324
Investments	41,426	37,130
Receivables from Allergan	3,501	—
Prepaid expenses and other receivables	1,916	1,389
Other assets	207	207
Total current assets	147,370	73,050
Property and equipment, net	2,678	2,092
Investments	15,050	3,712
Other assets	598	824
Total assets	$ 165,696	$ 79,678
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,367	$ 4,003
Accrued expenses	7,955	2,214
Notes payable and capital leases	489	602
Total current liabilities	12,811	6,819
Capital leases – noncurrent	1,392	482
Other long-term liabilities	1,895	1,325
Total liabilities	16,098	8,626
Commitments and contingencies (Notes 7-11)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 2,000 shares authorized; no shares issued and outstanding, respectively	—	—
Common stock, $0.001 par value, 60,000 shares authorized; 41,845 and 31,847 shares issued and outstanding, respectively	42	32
Additional paid-in capital	321,189	198,393
Accumulated other comprehensive loss	(470)	(279)
Accumulated deficit	(171,163)	(127,094)
Total stockholders' equity	149,598	71,052
Total liabilities and stockholders' equity	$ 165,696	$ 79,678

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

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)

	Year Ended December 31,		
	2004	2003	2002
Revenues:			
Revenues from product co-promotion	$ 11,068	$ —	$ —
Collaborative research agreements	—	5,200	4,883
Total revenue	11,068	5,200	4,883
Operating expenses:			
Research and development	25,698	27,631	25,229
Selling and marketing	21,848	2,838	60
General and administrative	9,041	7,002	5,091
Total operating expenses	56,587	37,471	30,380
Loss from operations	(45,519)	(32,271)	(25,497)
Other income (expense):			
Interest income	1,765	1,262	878
Interest expense	(117)	(46)	(74)
Loss on investments	(198)	(340)	—
Other income	1,450	876	804
Net loss	$(44,069)	$(31,395)	$(24,693)
Basic and diluted net loss per common share	$ (1.25)	$ (1.03)	$ (0.96)
Common shares used in computing basic and diluted net loss per common share	35,261	30,526	25,821

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

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2004	2003	2002
Cash flows from operating activities:			
Net loss	$ (44,069)	$(31,395)	$(24,693)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization expense	207	399	1,073
Depreciation of fixed assets	907	680	633
(Gain)/loss on disposal of property and equipment	(9)	80	6
Loss on investments	198	340	—
Changes in operating assets and liabilities:			
Receivables from Allergan	(3,501)	—	—
Prepaid expenses and other receivables	(527)	(553)	(99)
Other assets	19	(993)	(15)
Accounts payable	364	3,079	(217)
Accrued expenses	6,311	2,602	(430)
Deferred revenue	—	(2,200)	(1,883)
Net cash used in operating activities	(40,100)	(27,961)	(25,625)
Cash flows from investing activities:			
Purchase of investments	(72,978)	(74,933)	(12,306)
Proceeds from sale of investments	56,955	38,487	35,700
Increase in restricted deposits	—	(515)	—
Purchase of property and equipment	—	(1,193)	(229)
Proceeds from sale of property and equipment	61	5	—
Net cash (used) provided by investing activities	(15,962)	(38,149)	23,165
Cash flows from financing activities:			
Issuance of common stock, net	122,806	73,330	25
Proceeds from notes payable	—	619	—
Payments on notes payable and capital lease obligations	(748)	(643)	(396)
Net cash provided (used) by financing activities	122,058	73,306	(371)
Increase (decrease) in cash and cash equivalents	65,996	7,196	(2,831)
Cash and cash equivalents, beginning of period	34,324	27,128	29,959
Cash and cash equivalents, end of period	$100,320	$ 34,324	$ 27,128

Supplemental disclosure of non-cash investing and financing activities: The Company made cash payments for interest of $119, $42 and $73 for the years ended December 31, 2004, 2003 and 2002, respectively. The Company acquired property and equipment through the assumption of capital lease obligations amounting to $1,545 and $603 during the years ended December 31, 2004 and 2003, respectively.

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

INSPIRE PHARMACEUTICALS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock		Additional			Accumulated Other	
	Number of Shares	Amount	Paid-In Capital	Accumulated Deficit	Deferred Compensation	Comprehensive (Loss)/income	Stockholders' Equity
Balance at December 31, 2001	25,752	$ 26	$125,099	$ (71,006)	$(1,525)	$ 1	$ 52,595
Issuance of common stock	103	—	25	—	—	—	25
Forfeiture of common stock options	—	—	(55)	—	55	—	—
Amortization of deferred compensation	—	—	—	—	1,071	—	1,071
Net loss	—	—	—	(24,693)	—	—	(24,693)
Balance at December 31, 2002	25,855	26	125,069	(95,699)	(399)	1	28,998
Issuance of common stock	5,992	6	73,324	—	—	—	73,330
Amortization of deferred compensation	—	—	—	—	399	—	399
Unrealized (loss) on investments	—	—	—	—	—	(280)	(280)
Net loss	—	—	—	(31,395)	—	—	(31,395)
Balance at December 31, 2003	31,847	32	198,393	(127,094)	—	(279)	71,052
Issuance of common stock	9,998	10	122,796		—	—	122,806
Unrealized (loss) on investments	—	—	—	—	—	(191)	(191)
Net loss	—	—	—	(44,069)	—	—	(44,069)
Balance at December 31, 2004	41,845	$ 42	$321,189	$(171,163)	$ —	$(470)	$149,598

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

1. Organization

Inspire Pharmaceuticals, Inc. (the "Company", or "Inspire") was incorporated in October 1993 and commenced operations in March 1995 following the Company's first substantial financing and licensing of the initial technology from The University of North Carolina at Chapel Hill ("UNC"). Inspire is located in Durham, North Carolina, adjacent to the Research Triangle Park.

Inspire has incurred losses and negative cash flows from operations since inception. The Company expects it has sufficient liquidity to continue its planned operations beyond 2006, but also expects that additional capital may be required. Continuation of its operations beyond 2006 will require the Company to: (1) obtain product candidate approvals, (2) in-license commercial products, (3) obtain additional co-promotion agreements, and/or (4) raise additional capital through equity or debt financings or from other sources. The Company began receiving revenue from its co-promotion of Elestat™ and Restasis® in 2004, but will continue to incur operating losses until co-promotion and/or product revenues reach a level sufficient to support ongoing operations.

2. Summary of Significant Accounting Policies and Concentrations of Risk

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results will differ from those estimates.

Cash, Cash Equivalents, Interest and Other Receivables

The Company considers all highly-liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The carrying value of cash, cash equivalents, interest and receivables approximate their fair value due to the short-term nature of these items.

Investments

Investments consist primarily of United States government and government agency obligations, money market investments, municipal notes and bonds and asset or mortgage-backed securities. The Company invests in high-credit quality investments in accordance with its investment policy which minimizes the possibility of loss. Investments with original maturities at date of purchase beyond three months and which mature at or less than twelve months from the balance sheet date are classified as current. The Company has investments in auction rate securities which have long-term stated maturities of 20 to 30 years. However, these securities have characteristics of short-term investments due to a rate-setting mechanism and the ability to liquidate these securities through a Dutch auction process that occurs on predetermined intervals of 90 days or less. Accordingly, the Company classifies auction rate securities with these maturity re-set dates within twelve months of the balance sheet date as short-term as this corresponds to management's intention and the liquid nature of these securities. Generally, investments with a maturity beyond twelve months from the balance sheet date are classified as long-term. Investments are considered to be available-for-sale and are carried at fair value with unrealized gains and losses recognized in other comprehensive income (loss). Realized gains and losses are determined using the specific identification method and transactions are recorded on a settlement date basis. Marketable and non-marketable equity investments are evaluated periodically for impairment. If it is determined that a decline of any investment is other than temporary, then the investment would be written down to fair value and the write-down would be

included in the Company's operating results as a realized loss. Since the Company's investment policy requires it to purchase high-quality marketable securities with a maximum individual maturity of three years and requires an average portfolio maturity of no more than one year, the caliber and short-term nature of its marketable securities generally avoid other than temporary impairment.

The Company has an equity investment in Parion Sciences, Inc. ("Parion"), a non-public entity for which its fair value is not readily determinable. For this investment in which the Company does not have significant influence and owns less than 5% of Parion, the investment is carried at cost and is subject to a write-down for impairment whenever events or changes in circumstances indicate that the carrying value may not be recoverable. In 2003, the Company wrote-down the value of its investment in Parion and recognized a loss of $300. As of December 31, 2004 and 2003, this investment's recorded value was $200.

Property and Equipment

Property and equipment is primarily comprised of furniture, software, laboratory and computer equipment which are recorded at cost and depreciated using the straight-line method over their estimated useful lives which range from three to seven years. Leased property and equipment, which includes certain equipment under capital leases, and leasehold improvements are depreciated over the shorter of the lease period or their estimated useful lives.

The carrying values of property and equipment are periodically reviewed to determine if the facts and circumstances suggest that a potential impairment may have occurred. The review includes a determination of the carrying values of assets based on an analysis of undiscounted cash flows over the remaining depreciation period. If the review indicates that carrying values may not be recoverable, the Company will reduce the carrying values to the estimated fair value.

Restricted Deposits

Restricted deposits consist of cash and cash equivalents which collateralize a letter of credit that is required under the terms of a vehicle fleet financing agreement. Restricted deposits are classified as current or long-term based upon the expected release date of such restriction. The carrying amount of these restricted deposits approximates fair value. At December 31, 2004 and 2003, the Company had $515 of restricted deposits.

Intangible Assets

Costs associated with obtaining and maintaining patents on the Company's product candidates and license initiation and preservation fees, including milestone payments by the Company to its licensors, are evaluated based on the stage of development of the related product candidate and whether the underlying product candidate has an alternative use. Costs of these types incurred for product candidates not yet approved by the U.S. Food and Drug Administration ("FDA") and for which no alternative use exists are recorded as expense. In the event a product candidate has been approved by the FDA or an alternative use exists for a product candidate, patent and license costs are capitalized and amortized over the expected life of the related product candidate. License milestone payments to the Company's licensors are recognized when the underlying requirement is met.

Other Assets

During December 2003, the Company recorded a deferred charge associated with an up-front milestone payment made in conjunction with the Elestat™ co-promotion agreement executed in December 2003. This asset is amortized ratably on a straight-line basis through October 2008, the expected commercial exclusivity period

for Elestat™ in the United States. At December 31, 2004 and 2003, the Company had $793 and $1,000 of deferred charge associated with the up-front milestone, respectively, and $207 in accumulated amortization at December 31, 2004.

Revenue Recognition

The Company recognizes revenue from product co-promotion based on net sales for Elestat™ and Restasis®, as defined in the co-promotion agreements, and as reported to Inspire by its collaborative partner, Allergan, Inc. ("Allergan"). Accordingly, the Company's co-promotion revenue is based upon Allergan's revenue recognition policy, other accounting policies and the underlying terms of the co-promotion agreements. Allergan recognizes revenue from product sales when goods are shipped and title and risk of loss transfers to the customer. The co-promotion agreements provide for gross sales to be reduced by estimates of sales returns, credits and allowances, normal trade and cash discounts, managed care sales rebates and other allocated costs as defined in the agreements. The Company also reduces gross sales for incentive programs it manages, estimating the proportion of sales that are subject to such incentive programs and reducing revenue appropriately. Under the Elestat™ co-promotion agreement, the Company is obligated to meet predetermined minimum annual net sales performance levels. If the annual minimum is not satisfied, the Company records a reduced percentage of net sales based upon its level of achievement of predetermined calendar year net sales target levels. Amounts contractually due from Allergan in excess of recorded co-promotion revenue are recorded as deferred revenue.

The Company recognizes milestone revenue under its collaborative research and development agreements when Inspire has performed services under such agreements or when Inspire or its collaborative partner has met a contractual milestone triggering a payment to the Company. Non-refundable fees received at the initiation of collaborative agreements for which the Company has an ongoing research and development commitment are deferred and recognized ratably over the period of ongoing research and clinical development commitment. The Company is also entitled to receive milestone payments under its collaborative research and development agreements based upon achievement of development milestones by Inspire or its collaborative partners. The Company recognizes milestone payments as revenues ratably over the period of its research and development commitment. The recognition period begins at the date the milestone is achieved and acknowledged by the collaborative partner, which is generally at the date payment is received from the collaborative partner, and ends on the date that the Company has fulfilled its research and development commitment. This period is based on estimates by management and the progress towards milestones in the Company's collaborative agreements. The estimate is subject to revision as the Company's development efforts progress and the Company gains knowledge regarding required additional development. Revisions in the commitment period are made in the period that the facts related to the change first become known. This may cause the Company's revenue to fluctuate from period to period.

Research and Development

Research and development costs include all direct costs and indirect development costs related to the development of the Company's portfolio of product candidates. These expenses include: salaries for research and development personnel, consulting fees, clinical trial costs, sponsored research costs, clinical trial insurance, license fees and other fees and costs related to the development of product candidates. These costs have been charged to operating expense as incurred. License milestone payments to the Company's licensors are recognized when the underlying requirement is met.

(in thousands, except per share amounts)

Income Taxes

The Company accounts for income taxes using the liability method which requires the recognition of deferred tax assets or liabilities for the temporary differences between financial reporting and tax bases of the Company's assets and liabilities and for tax carryforwards at enacted statutory tax rates in effect for the years in which the differences are expected to reverse. The effect on deferred taxes of a change in tax rates is recognized in income in the period that includes the enactment date. In addition, valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized. If it is "more likely than not" that some portion, or all of a deferred tax asset will not be realized, a valuation allowance is recorded.

Deferred Compensation and Stock Options and Warrants

The Company accounts for deferred compensation based on the provisions of Accounting Principles Board Opinion No. 25 ("APB No. 25"), "*Accounting for Stock Issued to Employees*," which states that no compensation expense is recorded for employee stock options that are granted with an exercise price equal to or above the estimated fair value per share of the Company's common stock on the grant date. If stock options are granted with an exercise price below the estimated fair value of the Company's common stock, the difference is recorded as deferred compensation. The Company did not recognize any deferred compensation associated with stock option grants for the years ended December 31, 2004, 2003, and 2002.

Deferred compensation is amortized over the service period of the related stock option. The Company recognized $0, $399 and $1,071 of stock-based compensation expense related to amortization of deferred compensation during the years ended December 31, 2004, 2003 and 2002, respectively.

Statement of Financial Accounting Standards ("SFAS") No. 123, "*Accounting for Stock – Based Compensation*," ("SFAS No. 123"), as amended by SFAS No. 148, "*Accounting for Stock-Based Compensation – Transaction and Disclosure*" requires the Company to disclose pro forma information regarding option grants and warrants issued to its employees. In December 2004, the Financial Accounting Standards Board ("FASB") issued SFAS No. 123(R) "*Share-Based Payment*," which requires all share-based payments to employees, including any grants of employee stock options, to be recognized in the income statement based on their fair value for interim or annual reporting periods that begin after June 15, 2005. (See "Recent Accounting Pronouncements" below).

The Company has adopted the disclosure requirements of SFAS No. 123, which requires compensation expense be disclosed based on the fair value of the options granted at the date of the grant. For purposes of pro forma disclosures, the estimated fair value of equity instruments is amortized to expense over their respective vesting period. If the Company had elected to recognize compensation expense based on the fair value of stock-based instruments at the grant date, as prescribed by SFAS No. 123, its pro forma net loss and net loss per common share would have been as follows:

	Year Ended December 31,		
	2004	2003	2002
Net loss as reported	$(44,069)	$(31,395)	$(24,693)
Compensation expense included in reported net loss	—	399	1,071
Pro forma adjustment for compensation expense	(9,670)	(5,764)	(3,721)
Net loss —pro forma	$(53,739)	$(36,760)	$(27,343)
Net loss per common share—as reported	$ (1.25)	$ (1.03)	$ (0.96)
Net loss per common share—pro forma	$ (1.52)	$ (1.20)	$ (1.06)

(in thousands, except per share amounts)

To determine the impact of SFAS No. 123, the fair value of each option grant is estimated on the date of the grant using the Black-Scholes valuation model and the following assumptions:

	Year Ended December 31,		
	2004	2003	2002
Expected dividend yield	0%	0%	0%
Expected stock price volatility	110%	120%	136%
Risk free interest rate	3.33%	3.19%	3.82%
Expected life of options	5 years	5 years	5 years

Net Income (Loss) Per Common Share

Basic net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of common shares outstanding. Diluted net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of common shares and dilutive potential common share equivalents then outstanding. Potential common shares consist of shares issuable upon the exercise of stock options and warrants. The calculation of diluted earnings per share for the years ended December 31, 2004, 2003 and 2002 does not include 1,426, 1,624 and 750, respectively, of potential shares of common stock equivalents, as their impact would be antidilutive.

Accumulated Other Comprehensive Loss

Accumulated other comprehensive loss is comprised of unrealized gains and losses on marketable securities and is disclosed as a component of stockholders' equity. At December 31, 2004 and 2003, the Company had a $470 and $279 unrealized loss on its investments, respectively.

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

	2004	2003	2002
Net loss	$(44,069)	$(31,395)	$(24,693)
Reclassification adjustment for gains/losses in net loss	198	40	—
Change in unrealized gains/losses on investments	(389)	(320)	—
Total comprehensive loss	$(44,260)	$(31,675)	$(24,693)

Advertising

The Company engages in general and direct-response advertising when promoting and marketing Elestat™. These advertising costs are expensed as the costs are incurred. Advertising and product promotion expenses were $3,556 and $247 for the years ended December 31, 2004 and 2003, respectively. Advertising costs for the year ended December 31, 2002 were insignificant.

Significant Customers and Risk

All revenues recognized and recorded in 2004 and 2003 were from one collaborative partner. All revenues recognized and recorded in 2002 were from two collaborative partners. The Company is entitled to receive co-promotion revenue on "Net Sales" of Elestat™ and Restasis® under the terms of its collaborative agreements with Allergan, and accordingly, all trade receivables are concentrated with Allergan. Due to the nature of these agreements, Allergan has significant influence over the commercial success of these products.

Credit Risk

Cash equivalents and investments are financial instruments which potentially subject the Company to concentration of risk to the extent recorded on the balance sheet. Management of the Company believes it has established guidelines for investment of its excess cash relative to diversification and maturities that maintain safety and liquidity. To minimize the exposure due to adverse shifts in interest rates, the Company currently maintains a portfolio of investments with an average maturity of 12 months or less at December 31, 2004. The Company keeps all of its cash deposits in financial institutions in the United States.

Risks from third party manufacturing concentration

The Company relies on single source manufacturers for each of its products and product candidates. Accordingly, it has little control over the manufacture of products for which it will receive revenue and over the overall product supply chain.

Reclassifications

Certain prior year amounts have been reclassified to conform with the current year presentation.

Recent Accounting Pronouncements

In December 2004, the FASB issued SFAS No. 123(R) (revised 2004, or "SFAS No. 123(R)"), "*Share-Based Payment,*" a revision of FASB Statement No. 123 "*Accounting for Stock-Based Compensation.*" SFAS No. 123(R) supersedes APB No. 25, and amends SFAS No. 95, "*Statement of Cash Flows.*" SFAS No. 123(R) requires all share-based payments to employees, including grants of employee stock options, to be recognized in the income statement based on their fair values for all periods that begin after June 15, 2005. Pro forma disclosure will no longer be an alternative. (See "Deferred Compensation and Stock Options and Warrants" above for historic pro forma disclosure.) SFAS No. 123(R) permits public companies to adopt its requirements using one of two methods:

1. A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS No. 123(R) for all share-based payments granted after the effective date and (b) based on the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123(R) that remain unvested on the effective date; or

2. A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS No. 123 for purposes of pro forma disclosures either for (a) all prior periods presented or (b) prior interim periods of the year of adoption.

The Company intends to adopt SFAS No. 123(R) effective July 1, 2005. As permitted by SFAS No. 123, the Company currently accounts for share-based payments to employees using APB No. 25's intrinsic value method and, as such, generally recognizes no compensation cost for employee stock options. Accordingly, the adoption of SFAS No. 123(R)'s fair value method will have a significant impact on the Company's results of operations and its overall financial position. An estimate of the non-cash stock option expense for the last half of 2005, based upon the current number of stock options outstanding and calculated using assumptions and a valuation model consistent with 2004 quarterly filings, is approximately $5 million. However, actual expense may be materially different depending on the valuation model, assumptions and methodologies used in implementing SFAS No. 123(R), as well as the number of unvested stock options outstanding during 2005.

(in thousands, except per share amounts)

In March 2004, the FASB issued Emerging Issues Task Force ("EITF") Issue No. 03-13 ("EITF 03-13"), "Applying the Conditions in Paragraph 42 of FASB Statement No. 144 ("FASB No. 144"), *Accounting for the Impairment or Disposal of Long-Lived Assets,* in Determining Whether to Report Discontinued Operations." The FASB staff established a working group to assist in the development of a model for evaluating (a) which cash flows are to be considered in determining whether cash flows have been or will be eliminated and (b) what types of continuing involvement constitute significant continuing involvement. The Company has adopted FASB No. 144 and EITF 03-13 and they have not had a material impact on the Company's financial position, results of operations or cash flows.

In March 2004, the FASB issued EITF Issue No. 03-1 ("EITF 03-1"), *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments"* which provided new guidance for assessing impairment losses on investments. Additionally, EITF 03-1 included new disclosure requirements for investments that are deemed to be other-than-temporarily-impaired. The Company has adopted the disclosure requirements of EITF 03-1. In September 2004, the FASB delayed the effective date of application guidance on impairment of securities included within EITF 03-01 and is currently reconsidering conclusions reached in EITF 03-1.

In December 2003, the FASB issued Interpretation No. 46R ("FIN 46R"), "*Consolidation of Variable Interest Entities*," which replaces Interpretation No. 46. FIN 46R requires existing unconsolidated variable interest entities ("VIEs") to be consolidated by their primary beneficiaries if the entities do not effectively disperse risk among the parties involved. VIEs that effectively disperse risks will not be consolidated unless a single party holds an interest or combination of interest that effectively recombines risks that were previously dispersed. Application of FIN 46R is required in financial statements of public entities that have interest in VIEs or potential VIEs, commonly referred to as special-purpose entities, for periods after December 31, 2003. Application by public entities for all other types of entities is required in its financial statements for periods ending after March 31, 2004. The Company does not have interests in VIEs. FIN 46R did not have any impact on the Company's financial position, results of operations or cash flows.

3. Investments

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

	December 31,	
	2004	2003
United States Government and agencies	$27,432	$40,127
Auction rate securities	16,500	—
Corporate bonds	11,829	—
Restricted deposits	515	515
Preferred stock	200	200
	$56,476	$40,842

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

	December 31,	
	2004	2003
Less than one year	$41,426	$37,130
Greater than one year	14,335	2,997
	$55,761	$40,127

(in thousands, except per share amounts)

Gross realized and unrealized gains and losses on the Company's "available-for-sale" securities for the years ended December 31, 2004, 2003 and 2002 were not significant.

4. Property and Equipment

Property and equipment consist of the following:

	Useful Life (Years)	December 31, 2004	December 31, 2003
Equipment	5	$ 3,807	$ 3,004
Leasehold improvements	Lesser of lease term or 5 years	1,296	1,066
Computer hardware	3	931	761
Software	5	894	708
Furniture and fixtures	7	763	688
		7,691	6,227
Less—accumulated depreciation		(5,013)	(4,135)
Property and equipment, net		$ 2,678	$ 2,092

Depreciation expense was $907, $680 and $633 for the years ended December 31, 2004, 2003 and 2002, respectively. The Company leases certain assets under capital lease agreements. The net book value of assets under capital leases at December 31, 2004 and 2003 was approximately $1,621 and $677, respectively. Accumulated depreciation for assets under capital leases at December 31, 2004 and 2003 was $583 and $895, respectively.

5. Accrued Expenses

Accrued expenses are comprised of the following:

	December 31, 2004	December 31, 2003
Compensation and benefits	$4,088	$ 479
Development costs	1,555	1,112
Selling and Marketing costs	945	—
Duties and taxes	225	215
Other	1,142	408
	$7,955	$2,214

The carrying value of accrued expenses approximates fair value because of their short-term maturity.

(in thousands, except per share amounts)

6. Income Taxes

The Company had no federal, state or foreign income tax expense for the years ended December 31, 2004, 2003 and 2002.

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

	December 31,	
	2004	2003
Current deferred tax assets:		
Accrued expenses	$ 731	$ 561
Compensation related items	224	128
Noncurrent deferred tax assets:		
Domestic net operating loss carryforwards	59,417	42,828
Research and development credits	10,704	8,520
Fixed and intangible assets	1,817	1,607
Stock-based compensation	1,688	1,689
Contributions	286	220
Total deferred tax assets	74,867	55,553
Valuation allowance for deferred assets	(74,867)	(55,553)
Deferred tax assets	$ —	$ —

At December 31, 2004 and 2003, the Company has provided a full valuation allowance against its net deferred tax assets since realization of these benefits could not be reasonably assured. The increase in valuation allowance of $19,314 during the year ended December 31, 2004 resulted primarily from the generation of additional net operating loss carryforwards.

As of December 31, 2004, the Company had federal and state net operating loss carryforwards of $153,253 and $160,530, respectively. The net operating loss carryforwards expire in various amounts starting in 2008 and 2010 for federal and state tax purposes, respectively. The utilization of the federal net operating loss carryforwards may be subject to limitation under the rules regarding a change in stock ownership as determined by the Internal Revenue Code. If the Company's utilization of its net operating loss carryforwards is limited and the Company has taxable income which exceeds the permissible yearly net operating loss carryforward, the Company would incur a federal income tax liability even though its net operating loss carryforwards exceed its taxable income. Additionally, as of December 31, 2004 and 2003, the Company has federal research and development and orphan drug credit carryforwards of $10,704 and $8,520, respectively. The credit carryforwards expire in varying amounts starting in 2010.

Taxes computed at the statutory federal income tax rate of 34% are reconciled to the provision for income taxes as follows:

	Year Ended December 31,		
	2004	2003	2002
United States Federal tax at statutory rate	$(14,984)	$(10,674)	$ (8,396)
State taxes (net of Federal benefit)	(2,075)	(1,439)	(1,145)
Change in valuation reserve	19,314	13,290	12,269
Research and development credit	(2,184)	(2,044)	(3,033)
Nondeductible expenses due to credits	140	335	115
Other nondeductible expenses	(211)	532	190
Provision for income taxes	$ —	$ —	$ —

7. Stockholders' Equity

Sales of Common Stock

On August 2, 2000, the Company's Registration Statement on Form S-1, as amended, registering 6,325 shares of common stock, was declared effective by the Securities and Exchange Commission and permitted the Company to sell shares of common stock in its Initial Public Offering ("IPO"). On August 8, 2000, the Company sold 5,500 shares of common stock at the IPO for $12.00 per share which resulted in proceeds to the Company of $66,000. On September 5, 2000, the Company sold an additional 825 shares of common stock pursuant to the exercise by the underwriters of their over-allotment option with respect to such shares, generating additional gross proceeds of $9,900. Total stock issuance costs related to the IPO and exercise of the over-allotment option were $6,713.

In March 2003, the Company sold 5,750 shares of common stock, including the underwriters' over-allotment allocation, in a public offering at a price of $13.50 per share. The proceeds from the offering, net of applicable issuance costs and expenses, totaled approximately $72,600.

In July 2004, the Company sold 6,900 shares of common stock, including the underwriters' over-allotment allocation, in a public offering at a price of $12.00 per share. The proceeds from the offering, net of applicable issuance costs and expenses, totaled approximately $77,100. In November 2004, the Company sold 2,530 shares of common stock, including the underwriter's over-allotment allocation, in a public offering at a price of $17.10 per share. The proceeds from the offering, net of applicable issuance costs and expenses, totaled approximately $42,300.

The holders of common stock shall be entitled to receive dividends from time to time as may be declared by the Board of Directors, but a common stock dividend has never been declared, nor is a dividend payment expected in the near-term. The holders of shares of common stock are entitled to one vote for each share held with respect to all matters voted on by the stockholders of the Company.

Rights Agreement

In October 2002, the Company entered into a Rights Agreement with Computershare Trust Company. The Rights Agreement provides for a dividend of one preferred stock purchase right for each outstanding share of the Company's common stock. Each right entitles a stockholder, after the rights become exercisable, to buy 1/1,000th of a share of Inspire's Series H Preferred Stock at an exercise price of $50. Each right will become exercisable following the tenth day after an acquiring person or group acquires, or announces its intention to acquire, 15% or more of the common stock. The Company will be entitled to redeem the rights at $0.001 per right at any time on or before the close of business on the tenth day following acquisition by a person or group of 15% or more of the common stock. Under the Rights Agreement, if a person acquires 15% or more of the common stock without the approval of the Company's Board of Directors, all other stockholders will have the right to purchase securities from Inspire at a price that is less than its fair market value, which would substantially reduce the value of the common stock owned by the acquiring person. As a result, the rights will cause substantial dilution to a person or group that attempts to acquire the Company on terms not approved by the Company's Board of Directors, except pursuant to an offer conditioned on a substantial number of Rights being acquired. The rights should not interfere with any merger or other business combination approved by the Board of Directors since the rights may be redeemed by the Company at the redemption price of $0.001 prior to the occurrence of a distribution date.

(in thousands, except per share amounts)

8. Options and Warrants

Options

During 1995, the Company adopted the 1995 Stock Plan, which provided for the grant of up to 1,006 options to directors, officers, employees and consultants. In April 1999, the Plan was amended and restated, and is now the Amended and Restated 1995 Stock Plan, as amended (the "Plan"). The option pool was increased to 5,229 shares on September 28, 2001, to 6,429 shares on December 14, 2001 and to 7,179 on June 10, 2004. Under the Plan, both incentive and non-qualified stock options, as well as restricted stock, may be granted. The Board of Directors, or an appropriate committee of the Board of Directors, shall determine the terms, including exercise price and vesting schedule, of all options at their grant date, provided that for incentive stock options, such exercise price shall not be less than the fair market value of the Company's stock on the date of grant. At December 31, 2004, there were 473 options available for grant under the Plan.

The maximum term for an incentive stock option grant is ten years from the date of the grant. Options granted under the plan generally vest 25% upon completion of one full year of employment and on a monthly basis over the following three years. Vesting typically begins on the date of hire for new employees and on the date of grant for existing employees.

The following table summarizes the stock option activity for the Plan:

	Number of Shares	Weighted Average Exercise Price (per share)
Options outstanding, December 31, 2001	2,354	$ 6.931
Granted	970	3.379
Exercised	(103)	(0.240)
Forfeited	(96)	(8.947)
Options outstanding, December 31, 2002	3,125	5.985
Granted	1,443	17.386
Exercised	(237)	(2.985)
Forfeited	(118)	(4.960)
Options outstanding, December 31, 2003	4,213	10.092
Granted	1,227	14.447
Exercised	(308)	(4.472)
Forfeited	(218)	(12.574)
Options outstanding, December 31, 2004	4,914	$ 11.422

(in thousands, except per share amounts)

The following table summarizes information concerning options outstanding at December 31, 2004:

	Options Outstanding	Weighted Average Exercise Price (per share)	Weighted Average Remaining Contractual Life (in Years)	Options Exercisable
Exercise Price range (per share):				
$ 0.123 - $ 2.760	936	$ 1.308	5.84	759
$ 3.960 - $ 12.000	1,177	8.368	6.48	896
$ 12.250 - $ 13.650	912	13.111	8.09	365
$ 13.980 - $ 16.760	831	15.681	9.24	168
$ 16.860 - $ 20.000	792	18.514	8.75	248
$ 20.300 - $ 20.300	266	20.300	8.79	78
	4,914	$11.422	7.61	2,514

The weighted average exercise price (per share) of options granted during 2004, 2003 and 2002 was $14.447, $17.386 and $3.379, respectively.

SFAS No. 123, "Accounting for Stock-Based Compensation" requires the Company to disclose pro forma information regarding option grants made and warrants issued to its employees. See Note 2, "Summary of Significant Accounting Policies and Concentrations of Risk."

Common Stock Warrants

In connection with a collaboration agreement entered into with Genentech, Inc. ("Genentech") on December 17, 1999, the Company issued warrants to purchase shares of common stock at an exercise price of $7.88 per share, of which 254 were exercised on December 17, 2004 and the remainder expire on October 2, 2005. As of December 31, 2004 and 2003, a total of 25 and 285 warrants, respectively, were outstanding. During 2004 and 2003, 260 and 5 warrants, respectively, were exercised for shares of common stock.

9. Collaboration Agreements

On September 10, 1998, the Company entered into a Joint Development, License and Supply Agreement (the "Kissei Agreement") with Kissei Pharmaceutical Co. Ltd. ("Kissei") related to the development of INS365 Respiratory for all therapeutic respiratory applications, excluding sinusitis and middle ear infection, in Japan. Upon signing of the Kissei Agreement, Kissei purchased shares of the Company's preferred stock for $900 and the Company received a non-refundable up-front license fee of $3,600. The Company recognized this collaborative research revenue over the term of its research and development commitment, which ended in November 2002 as a result of the termination of the agreement. Upon termination of the agreement, Kissei returned all rights to INS365 Respiratory back to the Company.

On December 16, 1998, the Company entered into a Development, License and Supply Agreement (the "Santen Agreement") with Santen Pharmaceutical Co., Ltd. ("Santen") to complete the development of diquafosol for the therapeutic treatment of ocular surface diseases. Santen received an exclusive license to develop and commercialize diquafosol in Japan, China, South Korea, the Philippines, Thailand, Vietnam, Taiwan, Singapore, Malaysia and Indonesia in the field. The Company retains the right to manufacture and supply diquafosol in bulk drug substance form to Santen.

Under the terms of the Santen agreement, Inspire has received a total of $2,000 in equity and non-refundable milestone payments. Depending on whether all milestones under the Santen Agreement are met, the Company could receive milestone payments of up to $4,750. As of December 31, 2004, the Company had received $500 of these contingent development milestones. In addition, the Company will receive royalties on net sales of diquafosol by Santen, if any. No milestone payments were received under the Santen Agreement during 2004, 2003 or 2002.

The Santen agreement will terminate when all patents licensed under the agreement have expired. Either Santen or the Company may terminate the agreement if the other materially breaches the agreement. In addition, the Company has the right to terminate the agreement at any time, subject to the coordinating committee's review and arbitration, if the Company determines that Santen has not made reasonably sufficient progress in the development or commercialization of products. If Santen breaches the agreement, or if the Company terminates the agreement because Santen has not made sufficient progress, Santen's license will terminate. Santen will provide the Company with all data and information relating to the Company's products, and will assign or permit it to cross-reference all regulatory filings and approvals.

On December 17, 1999, the Company entered into a Development, License and Supply Agreement (the "Genentech Agreement") with Genentech to jointly develop INS365 Respiratory and other related $P2Y_2$ agonists existing on the date of the Genentech Agreement for all human therapeutic uses for the treatment of respiratory tract disorders, including chronic bronchitis and cystic fibrosis, throughout the world, excluding Japan and the treatment of sinusitis and middle ear infection worldwide.

Upon signing of the agreement, Genentech paid a non-refundable, non-creditable up-front payment of $5,000, purchased shares of preferred stock for $10,000 and was issued warrants. The Company recognized the $5,000 payment as collaborative research revenue over the term of the Company's research and development commitment, which ended in November 2001 as a result of the termination of the agreement. On December 20, 2000, upon achievement of a technical milestone, the Company sold shares of common stock to Genentech and issued additional warrants. Genentech returned all rights for use of INS365 Respiratory and other related $P2Y_2$ agonists back to the Company at no charge upon termination of the agreement.

On September 12, 2000, the Company entered into a License Agreement (the "Kirin Agreement") with Kirin Brewery Co., Ltd., Pharmaceutical Division ("Kirin") to complete the development and commercialization of INS316 Diagnostic to aid in the diagnosis of lung cancer. Upon the signing of the Kirin Agreement, the Company received a $2,000 non-refundable up-front license fee which the Company recognized as collaborative research revenue over the term of the Company's research and development commitment. Kirin terminated the agreement in September 2004.

In June 2001, the Company entered into a Joint License, Development and Marketing Agreement with Allergan to develop and commercialize diquafosol and granted the right to co-promote Allergan's Restasis®. This agreement was amended in December 2003, in connection with the execution of the Elestat™ co-promotion agreement to reduce the co-promotion revenue rates due on net sales of Restasis®. Under the terms of the amended agreement, Allergan obtained an exclusive license to develop and commercialize diquafosol worldwide, with the exception of Japan and nine other Asian countries covered by Inspire's agreement with Santen. In return, Inspire received an up-front payment of $5,000 on execution of the agreement and has received $6,000 in milestone payments. Inspire can also receive up to an additional $28,000 in milestone payments assuming the successful completion of all the remaining milestones. The Company will also receive co-promotion revenue from Allergan on sales of diquafosol, if any, and on worldwide sales of Allergan's Restasis®, excluding most larger Asian markets. The Company began receiving co-promotion revenue on net sales of Restasis® in April 2004.

The Company is responsible for conducting, in collaboration with Allergan, the Phase 3 clinical trials for diquafosol for dry eye disease and for United States New Drug Application filing and potential approval. Allergan is responsible for all other development activities under the agreement, including all development outside the United States and in its territories, and for ex-United States regulatory submissions, filings, and approvals relating to products. In addition, all development costs associated with a potential corneal wound healing indication for diquafosol are solely the Company's responsibility until such time, if any, that it receives an NDA approval of diquafosol. Allergan is responsible for all commercial costs except for the cost of Inspire's sales force in the United States. Allergan is required to use commercially reasonable efforts to conduct development, seek regulatory approvals and market and sell the products. The agreement will be in effect until all patents licensed under the agreement have expired, unless terminated earlier.

In October 2002, the Company entered into a study funding agreement with the Cystic Fibrosis Foundation Therapeutics, Inc. ("CFFT"), whereby the majority of the expenses for one Phase 2 INS37217 Respiratory proof-of-concept clinical trial were funded by the CFFT, but the Company also recorded the corresponding expenses and liabilities as the CFFT incurred these costs. This clinical trial was completed in 2004. If the Company receives FDA approval for INS37217 Respiratory for the treatment of cystic fibrosis, the Company will be obligated to pay a development milestone, and possibly a sales milestone, to the CFFT. The aggregate milestones under this agreement are approximately $16,000. As of December 31, 2004, and 2003, the Company has recorded $1,895 and $1,325 of contingent liabilities, respectively, in "Other long-term liabilities" associated with this agreement. If it does not receive FDA approval, the Company will have no financial obligation to the CFFT, including the Phase 2 clinical trial costs the CFFT funded on the Company's behalf.

In December 2003, the Company entered into an agreement with Allergan to co-promote Elestat™ to ophthalmologists, optometrists and allergists in the United States. Elestat™ was approved by the FDA in October 2003 for the prevention of itching associated with allergic conjunctivitis. Inspire has the primary responsibility for selling, promotional and marketing activities of Elestat™ in the United States and is responsible for the associated costs. Allergan records sales of Elestat™ and remains responsible for all other product costs. Allergan retains the licensing rights relating to promotion of Elestat™ to U.S. prescribers other than ophthalmologists, optometrists and allergists; but the Company has a right of first refusal to obtain such rights in the event Allergan decides to engage a third party to undertake such activities. Under the terms of the agreement, Inspire paid Allergan an up-front payment and Allergan pays co-promotion revenue to Inspire on U.S. net sales of Elestat™, except in the event that a third party is engaged by Allergan to promote Elestat™ to prescribers outside Inspire's field, in which case Inspire will be paid a proportionate share of U.S. net sales of Elestat™ based upon filled prescriptions written by ophthalmologists, optometrists and allergists. The Company began receiving co-promotion revenue on sales of Elestat™ in February 2004.

10. License Agreements

On March 10, 1995, the Company licensed the rights to the patent for a Method of Treating Lung Disease with Uridine Triphosphates which covers INS316 Diagnostic from UNC. In connection with this license agreement, the Company paid $65 in license initiation fees and issued 298 shares of common stock with an estimated value at the date of issuance of $36 or $0.12 per share and has agreed to make milestone payments totaling up to $1,000. As of December 31, 2004, the Company has paid $500 of these contingent milestones. A $10 license preservation payment was made during each of 2004, 2003 and 2002.

On September 1, 1998, the Company licensed the rights to the patents for a Method of Treating Cystic Fibrosis with Dinucleotides, a Method of Treating Bronchitis with Uridine Triphosphates and related compounds, and a Method of Treating Ciliary Dyskinesia with Uridine Triphosphates and related compounds, which cover

INS365 Respiratory, from UNC. In connection with this license agreement, the Company paid $15 in license initiation fees and issued 29 shares of common stock with an estimated value at the date of issuance of $90 or $3.15 per share and has agreed to pay milestone payments totaling $160. The Company has made license preservation payments of $5 in 2004, 2003 and 2002.

In January 2002, the Company licensed the rights to the patent for Composition and Method for Initiating Platelet Aggregation from UNC. In connection with this license agreement, the Company paid $25 in license initiation fees and has agreed to pay milestone payments totaling $50.

If the Company fails to meet performance milestones relating to the timing of regulatory filings or pay the minimum annual payments under its respective UNC licenses, UNC may terminate the applicable license. In connection with the license agreements with UNC, the Company has agreed to pay royalties based on net sales of certain Licensed Products (as defined in the license agreements). The Company enters into sponsored research and development and clinical trial agreements with UNC on an annual basis whereby direct and indirect costs, as defined, are reimbursed by the Company.

On November 2, 2004, the Company executed an exclusive license agreement with the Wisconsin Alumni Research Foundation ("WARF") under which WARF granted the Company an exclusive license under several patents, including three U.S. patents, for use in developing and commercializing new treatments for glaucoma. Under the terms of the agreement, Inspire will design and fund all future research, development, testing, regulatory filings and potential marketing activities related to any product developed from the license. Inspire has paid WARF an upfront licensing payment of $150, and will pay additional contingent payments of up to an aggregate of $1,800 upon the achievement of development milestones, and royalties on sales of any regulatory approved product utilizing the licensed patents. Unless terminated earlier, the agreement will expire on a country-by-country basis upon the expiration of the patents in such country. If the Company fails to pay the minimum annual payments under its license or commits any material breach of any other material covenant, as defined in the agreement, and fails to remedy such breach within 90 days of written notice, WARF may terminate the applicable license.

11. Debt and other Commitments

The Company is obligated under master capital lease agreements for furniture, equipment, and computers, for which the underlying furniture, equipment and computers serve as collateral. The lease terms under these master lease agreements expire 48 months from the date of inception and have interest rates ranging from 8.2% to 9.6%. The Company also has operating leases for vehicles, facilities and office equipment that extend through January 2009 and are subject to voluntary renewal options.

In addition, the vehicle lease agreement requires the Company to maintain a Standby Letter of Credit in the amount of $515 during the term of the lease for which an equivalent amount of the Company's cash and investments are held in a restricted account. The vehicle lease agreement also requires that the vehicles under lease serve as collateral for the obligation. Maintenance of the Standby Letter of Credit is subject to an annual review and, when necessary, the amount is subject to adjustment based on the obligation outstanding and the Company's financial position and operating results.

On August 25, 2003, the Company entered into a short-term financing agreement with a financial institution to finance certain insurance policy premiums, whereby $619 was financed for nine months at an annual percentage rate of 3.75%.

(in thousands, except per share amounts)

Facility rent expense for operating leases during 2004, 2003 and 2002 was $489, $363 and, $376, respectively.

Future minimum lease payments under capital and non-cancelable operating leases with remaining lease payments as of December 31, 2004 are as follows:

Year Ending December 31,	Capital Leases	Operating Leases
2005	$ 636	$ 887
2006	641	648
2007	641	71
Thereafter	276	22
Total minimum lease payments	2,194	$1,628
Less amount representing interest	313	
Present value of net minimum capital lease payments	1,881	
Less current portion of capital lease obligations	489	
Capital lease obligations, excluding current portion	$1,392	

The carrying value of the Company's debt obligations at December 31, 2004 and 2003 approximate their fair value as the interest rates on these obligations approximate rates available in the financial market at such dates.

The Company enters into contractual commitments or purchase arrangements with various clinical research organizations, manufacturers of active pharmaceutical ingredients and/or drug product as well as with others. The amount of these financial commitments totaled approximately $6,306 at December 31, 2004. In addition, the Company has other contractual commitments outside of drug development under arrangements which totaled approximately $1,272 at December 31, 2004. These amounts may vary dependent upon the results of underlying studies, the completion of studies and/or projects and certain other variable components that may yield a result that differs from management's estimate. As of December 31, 2004, the Company's existing license, collaboration and sponsored research agreements require future cash payments upon the achievement of future milestones. In the aggregate, these agreements require payments of up to $14,450 assuming the achievement of all development milestones and up to $4,000 assuming the achievement of all sales milestones. Amounts payable by the Company under these agreements are uncertain and are contingent on a number of factors, including the progress of its discovery and drug development programs, its ability to obtain regulatory approvals, and the commercial success of its approved products. Additionally, the Company is obligated to pay royalties on net sales, if any, of certain product candidates currently in its portfolio. Some of the Company's license agreements require minimum annual license preservation fees.

12. Employee Benefit Plan

The Company has adopted a 401(k) Profit Sharing Plan ("the 401(k) Plan") covering all qualified employees on August 1, 1995. Participants may elect a salary reduction of 1% or more up to the IRS allowed maximum as a tax-deferred contribution to the 401(k) Plan. The 401(k) Plan permits discretionary employer contributions. If employer discretionary contributions are implemented, participants will begin vesting 100% immediately in such contributions. In 2004, 2003 and 2002, the Company elected a safe harbor contribution at 3.0% of annual compensation. These safe harbor contributions total $455, $231 and $149 for the years ended December 31, 2004, 2003 and 2002, respectively.

(in thousands, except per share amounts)

13. Co-promotion Revenue by Product Line

The Company operates its business as one business segment. The Company derives all of its Elestat™ co-promotion revenue from product sales in the United States and predominantly all of its Restasis® co-promotion revenue from product sales in the United States.

	Year Ended December 31,		
	2004	2003	2002
Elestat™	$ 9,586	$—	$—
Restasis®	1,482	—	—
	$11,068	$—	$—

14. Quarterly Financial Data (unaudited)

2004	First	Second	Third	Fourth	Total
Revenue	$ 609	$ 2,948	$ 3,791	$ 3,720	$ 11,068
Net loss available to common stockholders	(12,428)	(9,692)	(10,150)	(11,799)	(44,069)
Net loss per common share—basic and diluted	$ (0.39)	$ (0.30)	$ (0.28)	$ (0.29)	$ (1.25)

2003	First	Second	Third	Fourth	Total
Revenue	$ 1,100	$ 4,100	$ —	$ —	$ 5,200
Net loss available to common stockholders	(7,747)	(6,618)	(7,942)	(9,088)	(31,395)
Net loss per common share—basic and diluted	$ (0.29)	$ (0.21)	$ (0.25)	$ (0.29)	$ (1.03)

15. Subsequent Events

On February 9, 2005, the Company announced results of a Phase 3 clinical trial of diquafosol for treatment of dry eye disease. In that clinical trial (109), diquafosol failed to demonstrate statistically significant improvement as compared to placebo for the primary endpoint of the incidence of corneal clearing. Improvement compared to placebo was achieved for a number of secondary endpoints. The Company has held preliminary discussions with the FDA concerning the mixed findings and the next steps in the development plan for diquafosol. Based on these discussions, the Company intends to file an amendment to its New Drug Application for diquafosol by the end of the second quarter of 2005.

On February 15, 2005, a purported class action complaint was filed in the United States District Court for the Middle District of North Carolina by Mirco Investors, LLC on behalf of itself and all other similarly situated investors against the Company and certain of its senior officers. The complaint alleges violations of sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Securities and Exchange Commission Rule 10b-5, and focuses on statements that are claimed to be false and misleading regarding a Phase 3 clinical trial of the Company's dry eye product candidate, diquafosol. The plaintiffs seek unspecified damages on behalf of a purported class of purchasers of Inspire's securities during the period from June 2, 2004 through February 8, 2005. On February 16, 2005, a similar complaint against the same defendants was filed by Richard and Susan Giorgino. In addition, on March 4, 2005, a similar complaint against the same defendants was filed by Kiah Sai Tan. It is possible that additional complaints may be filed in the future. The Company expects that these individual lawsuits will be consolidated into a single civil action. The Company intends to defend the litigation vigorously. As with any legal proceeding, it is difficult to predict the eventual outcome of pending lawsuits; however, an unfavorable resolution of these matters could materially affect the Company's business, future results of operations, financial position and/or cash flows.

On February 11, 2005, the Company's Chairman, W. Leigh Thompson, M.D., Ph.D., D.Sc., passed away following a chronic illness. Kenneth B. Lee, Jr. was subsequently appointed as Chairman of the Board on February 17, 2005.

Exhibit Index

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation. (Incorporated by reference to Exhibit 3.1 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation (Incorporated by reference to Exhibit 3.2 to the Company's Annual Report on Form 10-K filed March 26, 2002).
3.3	Certificate of Designations of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.3 to the Company's Annual Report on Form 10-K filed March 7, 2003).
3.4	Amended and Restated Bylaws, as adopted March 30, 2004. (Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on April 15, 2004).
4.1	Specimen Common Stock Certificate. (Incorporated by reference to Exhibit 4.1 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
4.2	Rights Agreement, dated as of October 21, 2002, between the Company and Computershare Trust Company, which includes the form of Certificate of Designation of Series H Preferred Stock of Inspire Pharmaceuticals, Inc. as Exhibit "A", the form of Rights Certificate as Exhibit "B" and the Summary of Rights to Purchase Preferred Stock as Exhibit "C" (Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on October 22, 2002).
10.1†	Amended and Restated 1995 Stock Plan, as amended. (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004).
10.2†	Form of Incentive Stock Option. (Incorporated by reference to Exhibit 10.2 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.3†	Form of Non-statutory Stock Option. (Incorporated by reference to Exhibit 10.3 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.4*	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and The University of North Carolina at Chapel Hill, dated March 10, 1995. (Incorporated by reference to Exhibit 10.7 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.5	Lease between Inspire Pharmaceuticals, Inc. and Imperial Center, Limited Partnership regarding Royal Center I, Durham, North Carolina, dated as of May 17, 1995, as amended. (Incorporated by reference to Exhibit 10.8 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.6	Lease Agreement between Inspire Pharmaceuticals, Inc. and Petula Associates Ltd. regarding Royal Center II, Durham, North Carolina, dated as of December 30, 1997. (Incorporated by reference to Exhibit 10.10 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.7	Sublease Agreement between ICAgen, Inc. and Inspire Pharmaceuticals, Inc. regarding premises located at 4222 Emperor Boulevard, Suite 500, Durham, North Carolina, dated September 22, 1997 and extension of Sublease Agreement dated February 14, 2000. (Incorporated by reference to Exhibit 10.11 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).

Exhibit Number	Description
10.8*	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and The University of North Carolina at Chapel Hill, dated September 1, 1998. (Incorporated by reference to Exhibit 10.12 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.9*	Development, License and Supply Agreement between Inspire Pharmaceuticals, Inc. and Santen Pharmaceutical Co., Ltd., dated as of December 16, 1998. (Incorporated by reference to Exhibit 10.15 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.10	Registration Rights Agreement between Inspire Pharmaceuticals, Inc. and Santen Pharmaceutical Co., Ltd., dated as of December 16, 1998. (Incorporated by reference to Exhibit 10.16 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.11	Warrant Agreement between Inspire Pharmaceuticals, Inc. and Genentech, Inc., dated as of December 17, 1999. (Incorporated by reference to Exhibit 10.22 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.12	Amended and Restated Investors' Rights Agreement among Inspire Pharmaceuticals, Inc. and the holders of Series A, B, E and G Preferred Stock of the Company dated as of December 17, 1999. (Incorporated by reference to Exhibit 10.23 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.13†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Donald Kellerman dated February 3, 2000. (Incorporated by reference to Exhibit 10.24 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.14†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Gregory J. Mossinghoff dated February 4, 2000. (Incorporated by reference to Exhibit 10.25 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.15†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Benjamin R. Yerxa dated February 4, 2000. (Incorporated by reference to Exhibit 10.26 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.16†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Christy L. Shaffer dated February 10, 2000. (Incorporated by reference to Exhibit 10.28 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.17†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Richard M. Evans dated February 10, 2000. (Incorporated by reference to Exhibit 10.30 to the Company's registration statement on Form S-1 (Registration No. 333-31174) which became effective on August 3, 2000).
10.18†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Mary Bennett dated February 27, 2001. (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 15, 2001).
10.19†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Joseph Schachle dated April 3, 2001. (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 10, 2001).

Exhibit Number	Description
10.20*	License, Development and Marketing Agreement between Inspire Pharmaceuticals, Inc. and Allergan, Inc., dated as of June 22, 2001. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 29, 2001).
10.21*	Study Funding Agreement, dated as of October 3, 2002, between Inspire Pharmaceuticals, Inc. and The Cystic Fibrosis Foundation Therapeutics, Inc. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 4, 2002).
10.22	First Amendment to Lease Agreement between Inspire Pharmaceuticals, Inc. and Royal Center Two IC, LLC for Royal Center Two, Durham, North Carolina, dated as of June 28, 2002. (Incorporated by reference to Exhibit 10.31 to the Company's Annual Report on Form 10-K filed March 7, 2003).
10.23	Third Amendment to Lease Agreement between Inspire Pharmaceuticals, Inc. and Royal Center One IC, LLC for Royal Center One, Durham, North Carolina, dated as of June 28, 2002. (Incorporated by reference to Exhibit 10.32 to the Company's Annual Report on Form 10-K filed March 7, 2003).
10.24	Underwriting Agreement by and between Inspire Pharmaceuticals, Inc. and Deutsche Bank Securities and U.S. Bancorp Piper Jaffray Inc. dated March 13, 2003. (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed on March 14, 2003).
10.25	Second Amendment To Lease between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC dated as of June 6, 2003. (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.26†	Form of Inspire Pharmaceuticals, Inc. Employee Stock Option Agreement. (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.27†	Form of Inspire Pharmaceuticals, Inc. Director Non-Statutory Stock Option Agreement. (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 11, 2003).
10.28*	First Amendment to License, Development and Marketing Agreement, dated December 8, 2003, between Inspire Pharmaceuticals, Inc. and Allergan, Inc. and Allergan Sales, LLC and Allergan Pharmaceuticals Holdings (Ireland) Ltd. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 9, 2003).
10.29*	Elestat (Epinastine) Co-Promotion Agreement, entered into as of December 8, 2003, by and between Allergan Sales, LLC and Inspire Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 1, 2004).
10.30†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Thomas R. Staab, II, dated May 16, 2003. (Incorporated by reference to Exhibit 10.35 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.31	Second Amendment to Sublease and Consent between ICAgen, Inc., Inspire Pharmaceuticals, Inc. and Imperial Center Partnership and Petula Associates, Ltd., dated August 13, 2003 (Incorporated by reference to Exhibit 10.36 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.32	Master Lease Agreement between GE Capital Fleet Services and Inspire Pharmaceuticals, Inc., dated as of November 18, 2003, and related documentation (Incorporated by reference to Exhibit 10.38 to the Company's Annual Report on Form 10-K filed March 12, 2004).
10.33	Master Security Agreement between General Electric Capital Corporation and Inspire Pharmaceuticals, Inc., dated as of November 12, 2003, and related documentation (Incorporated by reference to Exhibit 10.39 to the Company's Annual Report on Form 10-K filed March 12, 2004).

Exhibit Number	Description
10.34	Underwriting Agreement by and among Inspire Pharmaceuticals, Inc. and Morgan Stanley & Co. Incorporated, Deutsche Bank Securities Inc., Piper Jaffray & Co. and SG Cowen & Co., LLC dated July 26, 2004 (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed July 27, 2004).
10.35†	Agreement between Inspire Pharmaceuticals, Inc. and Christy Shaffer, effective as of March 29, 2004, regarding change in control (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004).
10.36†	Form of Change in Control Agreement for other executive officers (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004).
10.37	Third Amendment to Lease, dated as of August 4, 2004, between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on August 12, 2004.)
10.38	Fourth Amendment to Lease, dated as of August 4, 2004, between Inspire Pharmaceuticals, Inc. and Royal Center IC, LLC (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on August 12, 2004.)
10.39†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between the Company and R. Kim Brazzell, dated August 5, 2004 (Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed November 9, 2004).
10.40†	Amended and Restated Director Compensation Policy.
10.41†	Agreement between Inspire Pharmaceuticals, Inc. and Barry G. Pea, effective as of October 11, 2004, regarding change in control.
10.42†	Employee Confidentiality, Invention Assignment and Non-Compete Agreement between Inspire Pharmaceuticals, Inc. and Barry G. Pea, dated October 13, 2004.
10.43†	Transition Agreement between Inspire Pharmaceuticals, Inc. and Gregory J. Mossinghoff, dated October 28, 2004.
10.44**	Exclusive License Agreement between Inspire Pharmaceuticals, Inc. and the Wisconsin Alumni Research Foundation, effective November 2, 2004.
10.45	Underwriting Agreement, dated November 10, 2004, by and between Inspire Pharmaceuticals, Inc. and Deutsche Bank Securities Inc. (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed November 12, 2004).
10.46†	Inspire Pharmaceuticals, Inc. Change in Control Severance Benefit Plan (Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.47†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Christy L. Shaffer (Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.48†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Mary B. Bennett (Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.49†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Richard M. Evans (Incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.50†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Donald J. Kellerman (Incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed January 31, 2005).

Exhibit Number	Description
10.51†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Joseph K. Schachle (Incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.52†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Thomas R. Staab, II (Incorporated by reference to Exhibit 10.7 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.53†	Agreement regarding change in control, dated as of March 29, 2004, by and between Inspire Pharmaceuticals, Inc. and Benjamin R. Yerxa (Incorporated by reference to Exhibit 10.8 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.54†	Agreement regarding change in control, dated as of August 2, 2004, by and between Inspire Pharmaceuticals, Inc. and R. Kim Brazzell (Incorporated by reference to Exhibit 10.9 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.55†	Agreement regarding change in control, dated as of October 11, 2004, by and between Inspire Pharmaceuticals, Inc. and Barry G. Pea (Incorporated by reference to Exhibit 10.10 to the Company's Current Report on Form 8-K filed January 31, 2005).
10.56†	Form of Inspire Pharmaceuticals, Inc. Employee Stock Option Agreement.
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

* Confidential treatment has been granted with respect to a portion of this Exhibit.

** Confidential treatment has been requested with respect to a portion of this Exhibit.

† Denotes a management contract or compensation plan or arrangement required to be filed as an exhibit pursuant to Item 15(c) of this Form 10-K.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in the Registration Statement on Form S-3 (File No. 333-114517) and Form S-8 (File No. 333-56360) of Inspire Pharmaceuticals, Inc. of our report dated March 11, 2005 relating to the financial statements, management's assessment of the effectiveness of internal control over financial reporting and the effectiveness of internal control over financial reporting which is included in this Annual Report on Form 10-K.

/s/ PricewaterhouseCoopers LLP

Raleigh, North Carolina
March 11, 2004

Exhibit 31.1

INSPIRE PHARMACEUTICALS, INC.

CERTIFICATIONS

I, Christy L. Shaffer, certify that:

1. I have reviewed this annual report on Form 10-K of Inspire Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2005

/s/ CHRISTY L. SHAFFER

Christy L. Shaffer
Chief Executive Officer
(principal executive officer)

Exhibit 31.2

INSPIRE PHARMACEUTICALS, INC.

CERTIFICATIONS

I, Thomas R. Staab, II, certify that:

1. I have reviewed this annual report on Form 10-K of Inspire Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2005

/s/ THOMAS R. STAAB, II

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

Exhibit 32.1

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

In connection with the annual report of Inspire Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2004, as filed with the Securities and Exchange Commission (the "Report"), I, Christy L. Shaffer, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2005

/s/ CHRISTY L. SHAFFER

Christy L. Shaffer
Chief Executive Officer
(principal executive officer)

Exhibit 32.2

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

In connection with the annual report of Inspire Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2004, as filed with the Securities and Exchange Commission (the "Report"), I, Thomas R. Staab, II, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2005

/s/ THOMAS R. STAAB, II

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

CORPORATE INFORMATION

Corporate Profile:
Inspire is a biopharmaceutical company dedicated to discovering, developing and commercializing prescription pharmaceutical products in disease areas with significant commercial potential and unmet medical needs. Inspire has significant technical and scientific expertise in the therapy areas of ophthalmology and respiratory and is a leader in the field of P2 receptors which are important drug targets in various therapeutic areas, including ophthalmology, respiratory disease and cardiovascular disease. Inspire's U.S. specialty sales force promotes Elestat™ and Restasis®, ophthalmology products developed by Inspire's partner, Allergan, Inc.

Annual Meeting:
The Annual Meeting of Stockholders will be held on Friday, June 10, 2005 at 9:00 a.m. Eastern time at the North Carolina Biotechnology Center, Research Triangle Park, NC

Stockholder Information:
Contact Inspire at 919-941-9777 to obtain stockholder information and a copy of Inspire's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission, free of charge.

Independent Registered Public Accounting Firm:
PricewaterhouseCoopers LLP
150 Fayetteville Street Mall
Suite 2300
Raleigh, NC 27601
919-755-3000

Corporate Counsel:
Reed Smith LLP
Princeton Forrestal Village
Suite 250
136 Main Street
Princeton, NJ 08543

Corporate Information:
Inspire Pharmaceuticals, Inc.
4222 Emperor Boulevard, Suite 200
Durham, NC 27703
www.inspirepharm.com
919-941-9777
Fax 919-941-9797

Securities Information:
Exchange: NASDAQ National Market®
Symbol: ISPH

Transfer Agent:
Computershare Trust Company
350 Indiana Street, Suite 800
Golden, CO 80401
www.computershare.com
303-262-0600
Fax 303-262-0604

Board of Directors:

Kenneth B. Lee, Jr.,
Chairman, Inspire Pharmaceuticals, Inc.
General Partner, Hatteras BioCapital, L.L.C.

Kip A. Frey
Partner, Intersouth Partners
Professor of the Practice, Duke University

Richard S. Kent, M.D.
Chief Executive Officer & President
Serenex, Inc.

William R. Ringo, Jr.
Chief Executive Officer & President
Abgenix, Inc.

Christy L. Shaffer, Ph.D.
Chief Executive Officer
Inspire Pharmaceuticals, Inc.

Corporate Officers:

Christy L. Shaffer, Ph.D.
Chief Executive Officer

Mary B. Bennett
Executive Vice President
Operations and Communications

R. Kim Brazzell, Ph.D.
Senior Vice President
Ophthalmic Research and Development

Richard M. Evans, Ph.D.
Vice President
Pharmaceutical Development

Donald J. Kellerman, Pharm.D.
Senior Vice President, Development

Gregory J. Mossinghoff
President (resigned effective June 2005)

Barry G. Pea
Executive Vice President, Corporate Development and General Counsel

Joseph K. Schachle
Senior Vice President, Marketing and Sales

Thomas R. Staab, II
Chief Financial Officer and Treasurer

Benjamin R. Yerxa, Ph.D.
Senior Vice President, Discovery

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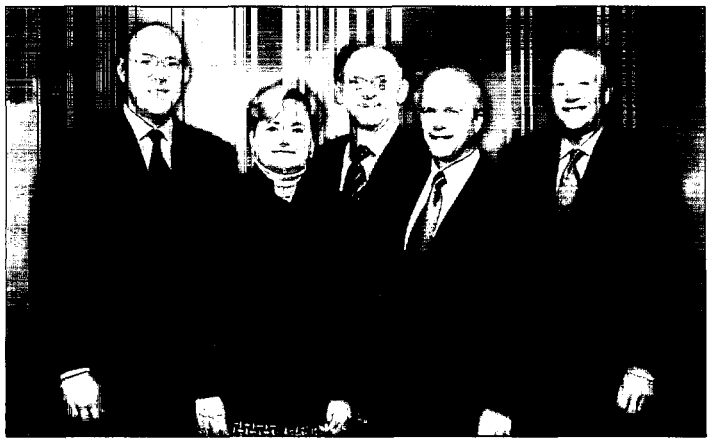

Board of Directors, as of April 2005 (left to right): Kip A. Frey, Christy L. Shaffer, Ph.D., William R. Ringo, Jr., Richard S. Kent, M.D., Kenneth B. Lee, Jr.

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