AVIGEN

2004 ANNUAL REPORT

Avigen 2004 Annual Report

Avigen's goal is to develop and commercialize innovative drugs for the treatment of chronic neurological conditions.

Avigen is shifting its focus from AAV-based gene therapy drug programs to the exclusive development of traditional pharmaceutical products. Avigen will continue to focus on building a strong neurologically-focused pipeline of drug development candidates comprised of small molecule therapeutics and biologics.

Avigen is currently working on multiple approaches to treat neuropathic pain, using both proprietary nonviral-based gene therapy technologies and new and existing classes of small molecule formulations. Each of these approaches are based on a promising new understanding and approach to treating pain which is gaining broad acceptance by researchers in the field. This approach focuses on the role of glial cells rather than traditional cell targets which have yet to create satisfactory treatments for neuropathic pain.

To Our Stockholders

Philip J. Whitcome, Ph.D.
Chairman of the Board

Kenneth G. Chahine, Ph.D., J.D.
President & Chief Executive Officer

In 2004, we made the strategic decision to reevaluate our emphasis on gene therapy in light of an increasingly challenging regulatory and clinical environment, and to begin to pursue a commercial strategy focused on small molecule pharmaceuticals and biologics to treat serious and chronic neurological disorders. Our decision to shift our research efforts was supported by many developments within the organization, including the recruitment of an experienced management team with broad development and commercialization experience, the strengthening of our neuropathic pain preclinical programs, the need to reduce our operating expenses, our efforts to search for and evaluate promising acquisition candidates and the reduction of our funding of AAV gene therapy. While this decision was difficult, it was necessary to allow Avigen to work unencumbered to build a sustainable business within acceptable capital and time constraints. We expect 2005 to be a year in which we establish Avigen as a company on its way to becoming a successful commercial enterprise.

Early in 2004 we provided guidance to stockholders that the regulatory and clinical environment surrounding gene therapy was challenging. We tried to adapt to the uncertain environment by shifting our focus to chronic diseases afflicting patients with few therapeutic alternatives, in order to improve the risk benefit profiles and promote faster development timelines for our programs. Unfortunately, this effort was insufficient to overcome the unfavorable sentiment and news flow surrounding the field of gene therapy. Increasing regulatory concerns over gene therapy have severely limited our ability to initiate and carry on a clinical trial in a timely and cost effective manner. After much discussion and deliberation we made the decision that Avigen could not sustain the risk and uncertainty surrounding the clinical development of gene therapy products.

Faced with such an environment, we made the strategic decision to curtail the funding of AAV-based programs and build a business based on small molecule and biological pharmaceutical products with an emphasis in neurology. We believe this builds on the clinical and development strengths of our senior staff, whose experience includes the development, testing and marketing of such neurological products.

The company is now focusing on creating a sustainable business built on our internal programs in neuropathic pain as well as the acquisition of molecules, preferably in later stage clinical development, in other neurological indications. Preclinically, we continue to work on a new and promising class of molecules for the treatment of chronic pain based on the pioneering work of scientists at

the University of Colorado and others whose work involves new discoveries concerning key factors that contribute to the origin and maintenance of a chronic pain state. We have evaluated several preclinical candidates and will be working in the coming year to identify the most promising candidates to advance into human clinical testing.

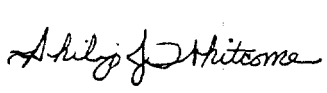
We are actively pursuing the acquisition or in-license of related neurological products in advanced clinical development and we are confident we have the expertise to identify and evaluate promising candidates. Avigen brings a strong development team, a solid financial position, sales and marketing expertise, and promising preclinical programs to compliment this effort.

In order to fulfill Avigen's mission we recognized the need to conserve our existing resources to support the small molecule pharmaceutical programs. To this end, we made the decision to substantially curtail our internal funding, while still exploring the opportunities for external support, of AAV-related expenses. Despite our determination that this strategic decision is right for our company, we continue to believe in the long-term potential of the AAV technology. We also believe that the scientific hurdles currently facing gene therapy will eventually be resolved, simply not within a timeframe which would make it a commercially viable alternative for Avigen. Avigen remains committed to facilitating the continued development of these programs through external sources, while maintaining an interest in its future commercial potential. Accordingly, we intend to place the technology in the best hands possible to ensure its continued development and support.

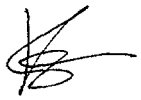
We are currently assessing a variety of options that are structured to allow us to meet our three strategic objectives of substantially reducing expenses, retaining downstream economic participation in the AAV technology, and providing for the continuation our ongoing clinical programs.

The company is in a strong financial position. We ended 2004 with approximately $76 million in cash, cash equivalents and investments. As we limit our spending on AAV-based programs, we expect our annualized net cash burn to be reduced by approximately 40% from the 2004 level of $23 million to an annualized rate of approximately $13 million. These financial projections do not include any estimates of expenses we will incur to complete an acquisition or the operating expenses that will be incurred to advance any acquired or in-licensed products through clinical development. It has been a difficult year for the company, but Avigen has emerged with a strong cash position and sharp focus on developing a commercial enterprise.

We want to thank our stockholders and employees for supporting our efforts over the last year and we look forward to sharing our progress and success with each of you during the coming year.



Philip J. Whitcome, Ph.D.
Chairman of the Board



Kenneth G. Chahine, Ph.D., J.D.
President and Chief Executive Officer

Forward-looking statements:
The statements made in this Annual Report regarding Avigen's plans and expectations for the future, including its new strategy, its expectations regarding acquiring new potential products, its expectations for its AAV technology, and its projected financial cash burn, are forward-looking statements subject to risks and uncertainties. Please see the risks outlined under "Risk Factors" in "Item 1. Business" of Avigen's Annual Report on Form 10-K for the fiscal year ended December 31, 2004, which is included as part of this Annual Report, for factors that could cause these forward-looking statements not to come true.

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

FORM 10-K

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

For the fiscal year ended December 31, 2004
OR

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

For the transition period from to _____ to _____.

Commission file number 0-28272

AVIGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware	**13-3647113**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*

1301 Harbor Bay Parkway
Alameda, California 94502
(Address of principal executive offices and zip code)

(510) 748-7150
(Registrant's telephone number, including area code)

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

Securities registered pursuant to Section 12(g) of the Act:
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 Sections 13 of 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 amendments to this Form 10-K. ☒

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes ☒ No ☐

The aggregate market value of the Common Stock held by non-affiliates of the registrant as of June 30, 2004, was approximately $55,300,000 based upon the closing sale price of the registrant's Common Stock as reported on the NASDAQ National Market on such date(1).

The number of outstanding shares of the registrant's Common Stock as of March 1, 2005, was 20,381,250 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the 2005 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K, are incorporated by reference in Part III, Items 10-14 of this Form 10-K.

(1) Excludes approximately 3,960,000 shares of the registrant's Common Stock held by directors and executive officers of the registrant, and by each person known by the registrant to own 5% or more of the registrant's outstanding Common Stock at June 30, 2004. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, directly or indirectly, to direct or cause the direction of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant.

ANNUAL REPORT ON FORM 10-K

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2004

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INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These statements are based upon current expectations that involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to:

- our intention to acquire or in-license drug candidates from third parties;
- our expectations related to acquiring or in-licensing drug candidates with prior experience in human clinical trials;
- the potential of our product development programs, including AV201 for Parkinson's disease;
- our expectations related to accelerating the pace of our AV201 clinical trial as a result of receiving clearance from the FDA to simultaneously enroll the remaining subjects in the first dose level;
- the expectations related to entering into an agreement with a collaboration partner that will provide significant funding for our gene-delivery based product development programs, including AV201 for Parkinson's disease;
- our intention to submit an IND to the FDA regarding our AV333 potential product;
- our expectations as to when we will file investigational new drug applications for acquired or in-licensed drug candidates or our other product candidates currently in preclinical development;
- our expectations with respect to the clinical development of our product candidates, our clinical trials and the regulatory approval process;
- our expectations as to the various products that we are developing;
- our expectations relating to our selection of additional disease targets;
- our expectations with regard to our future operational and manufacturing capabilities; and
- our estimates regarding our capital requirements, how long our current capital resources will last, and our needs for additional financing.

We have identified the forward-looking statements we make by using terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "potential" and similar expressions which imply that the statements relate to future events or expectations. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk Factors," in Item 1 below. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this Form 10-K.

You should read this Form 10-K and the documents that we incorporate by reference completely and with the understanding that our actual future results may be materially different from what we currently expect. We may not update these forward-looking statements, even though our situation may change in the future. We qualify all of our forward-looking statements by these cautionary statements.

PART I

Item 1. Business

Overview

Avigen is focused on acquiring, developing and commercializing innovative therapeutics to treat serious disorders, primarily for neurological conditions. The Company is shifting its focus from DNA-based drugs to more conventional small molecule therapeutics. We believe that our senior management team, with extensive small molecule development and commercialization experience, along with our current financial resources and status as a public company, creates a compelling opportunity for us, and puts Avigen in a unique position to attract promising late-stage drug candidates for the treatment of neurological disorders. We are actively seeking to identify and acquire rights to product candidates in later-stage clinical development with good human safety and efficacy data and hope to complete one or more transactions in 2005. We are also actively exploring opportunities to internally or externally maximize the value of our gene therapy assets, which are primarily based on our adeno-associated virus (AAV) vectors.

During the past ten years, we have built a product development portfolio of DNA-based drug delivery technologies, including our proprietary gene-delivery platform based on AAV vectors. To date, we have devoted our resources to early stage research in the field of gene therapy, which has led to our filing of three separate Investigational New Drug filings (INDs) and our initiation of three corresponding phase I or phase I/II clinical trials. These INDs and clinical trials used Avigen's AAV-based product candidates to treat hemophilia and Parkinson's disease.

Gene therapy has proven to be a challenging field. Despite our numerous discoveries and accomplishments, our development programs have uncovered new scientific challenges and the pace of our clinical trials continues to face uncertain regulatory review requirements from the United States Food and Drug Administration (FDA) and other agencies. Together, these factors have led to our strategic decision to restructure our portfolio of product candidates and focus on acquiring or licensing rights to more conventional pharmaceutical candidates. Management continues to restructure the company's operations to reduce our emphasis on our historically funded gene delivery programs.

Our Strategy

Our goal is to develop innovative therapeutic products for neurological disorders, and to commercialize these opportunities with our own financial resources, while maximizing the potential value of our past investment in gene delivery products. Key elements of our strategy to accomplish this goal are to:

- assemble a team of highly talented senior managers with experience in small molecule pharmaceutical development, sales and marketing;
- identify and acquire later-stage small molecule drug candidates that complement our neurological expertise and focus;
- continue research and preclinical development on proprietary product candidates in large markets with unmet medical needs such as neuropathic pain;
- fund and manage the clinical-stage development of our products;
- build a marketing infrastructure for distribution of our products in the U.S.;
- partner selectively with larger pharmaceutical companies to develop and co-promote our products outside the U.S.; and
- assess ongoing strategies to maximize the value of our past investment and achievements with AAV vectors and other gene delivery technologies.

We believe that our success will be dependent on our ability to retain the rights, when feasible, to commercialize our own products in the U.S. However, clinical development and commercialization requires sizable financial resources and Avigen may consider opportunities to acquire technologies that may involve sharing marketing rights in the U.S., if we believe that such opportunities have the potential to generate revenues in the near future that could

be used to offset our development expenses on other components of our product portfolio. To further our goal of commercializing our own products, we have recently expanded our management team with the addition of Michael Coffee as Chief Business Officer. Mr. Coffee has worked in marketing and executive management capacities, including president and chief operating officer, at various pharmaceutical companies in which he helped identify, acquire, and launch a number of successful pharmaceutical products. Mr. Coffee has also successfully established marketing organizations in the U.S. similar to the profile we expect will be required by our potential products. We intend to pursue opportunities to commercialize our products outside the U.S. through collaboration with partners that would have significantly greater clinical development and commercialization resources than ourselves.

In summary, we believe that our efforts to acquire later-stage clinical development candidates with human safety and efficacy data will enable us to most efficiently apply our scientific knowledge, management expertise, and financial resources to build a sustainable business and increase shareholder value.

Our History

Avigen, Inc. is a Delaware corporation that was incorporated on October 22, 1992 and is based in the San Francisco Bay Area. Since our inception, we have primarily focused our research and development activities on product candidates using our proprietary AAV vector gene delivery platform, and have initiated three phase I clinical trials under three FDA approved INDs. During the past year, in response to the information obtained from our clinical trials for hemophilia and our assessment of the near-term potential for timely clinical development in the field of gene therapy and our limited financial resources, our management has taken steps to implement a strategy of acquiring later-stage clinical development products of more conventional pharmaceuticals.

In May 2004, we suspended subject enrollment in our phase I clinical trial for hemophilia B in order to focus our development efforts and resources on our other development programs for neurological disorders. This suspension of the trial and realignment toward neurological disorders was intended to make the best use of our financial and scientific resources. In July 2004, in response to these strategic changes, we reduced our staff level by 37 employees, or approximately 36%. This reduction was seen as a critical step to extending our financial resources available for other programs, while retaining core competencies in AAV gene delivery technology.

In August 2004, we received authorization from the FDA to initiate a phase I/II clinical trial of AV201, our drug candidate for the treatment of Parkinson's disease, and in December 2004 we enrolled and treated our first subject. This clinical trial is designed to evaluate the safety of increasing doses of AV201 in individuals with mid-to-late stage Parkinson's disease. Clinical evaluations and positron emission tomography (PET) imaging will be used to assess preliminary efficacy. The currently approved version of this clinical trial protocol includes frequent health monitoring of the participants over the course of the first twelve months. In February 2005, after reviewing the results of our initial subject treatment with the FDA, we received clearance from the FDA to simultaneously enroll the remaining subjects in the first dose level, which we expect will result in an overall acceleration of our AV201 clinical trial.

In December 2004, we announced the termination of our collaboration agreement with Bayer Corporation. Under the agreement entered into in November 2000, Bayer, in collaboration with Avigen, had agreed to conduct any phase II/III clinical trials for our hemophilia product in exchange for exclusive worldwide marketing and distribution rights to any resulting products. In August 2004, both parties agreed that Avigen had met all of its contractual obligations required under the agreement to develop and market Coagulin-B for hemophilia B. As a result of the termination, Bayer no longer has any financial obligations to finance phase II/III development of the product and all patent and know-how rights licensed to Bayer revert back to Avigen. Since we were solely responsible for funding the phase I development, the termination had no immediate financial impact on us. In addition, as a result of the termination, we have the right to develop a product for the treatment of hemophilia B independently or in collaboration with another corporate partner in the future.

Business Development

We intend to pursue aggressively the acquisition or in-licensing of later-stage clinical development products in order to restructure and broaden our current portfolio. To date, our efforts have identified several compounds as candidates, some of which are currently in later-stage human clinical trials. As of March 1, 2005, we have not entered into any definitive agreements and continue to pursue opportunities that we believe best complement our

strategy and offer the potential to maximize our value to our shareholders. Competition for products in later-stage clinical development is intense and may require significant resources to obtain. If we are able to identify and negotiate the acquisition or in-licensing of compounds in later-state development, we may fund such transactions with the issuance of additional equity securities, which may further dilute our existing stockholders. There is no assurance that we will be successful in acquiring such products, or that such products can be acquired on terms acceptable to us.

Strategic Relationships

Research and commercial collaborations will continue to play a role in our business strategy. We will continue to pursue strategic relationships with leaders in the field that we feel could enhance the potential success of our portfolio of products. For example, we believe that collaborations with partners or other investors could provide extended financing and other critical resources that will be necessary to meet the demands of a longer and more complex development process for our gene delivery products. We have historically sought to partner our gene delivery products after they had entered the clinical trial phase in order to support our retention of a larger interest in their potential commercial value. In 2004, our AV201 product for Parkinson's disease met this milestone, and we will continue to pursue potential partners to support the continued development, and future marketing and distribution for, the potential product.

As we identify and acquire access to new development products, we will continue to evaluate opportunities to increase the potential success of these investments through strategic relationships, most likely with regard to development and marketing rights outside the U.S. We may also gain access to new development programs through collaboration agreements in which we obtain development and commercialization rights in the U.S. from a third-party. If we are able acquire access to compounds through strategic relationships, we may fund such transactions with the issuance of additional equity securities, which may further dilute our existing stockholders.

If we are successful in acquiring new products, we may not have the capabilities to manufacture any one or more, or any of, the new products. As a result, we may need to rely significantly on supply agreements with third-party manufacturers to manufacture drug substances and final drug products for both clinical development and commercial sale.

Bayer Corporation. In November 2000, we had entered into a collaboration agreement with Bayer Corporation in connection with the development of Coagulin-B, our gene therapy product for hemophilia. Under the terms of the agreement, Bayer intended to conduct any Phase II/III clinical trials for Coagulin-B in exchange for exclusive worldwide marketing and distribution rights to any resulting products. In May 2004, we mutually agreed to suspend the phase I clinical study of Coagulin-B and in December 2004, Bayer formally terminated the collaboration agreement between itself and Avigen.

Gene Delivery Product Development Programs

Our current gene delivery product development programs, which have progressed beyond early research stages, are:

Product Candidate	Disease	Protein/Enzyme	Target Tissue	Phase of Development
AV201	Parkinson's disease	Aromatic amino acid decarboxylase (AADC)	Brain	phase I/II clinical trial
AV333	Neuropathic pain	Interleukin-10 (IL-10)	Spinal cord	Preclinical

Parkinson's Disease

The Disease

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease. Signs and symptoms of the disease include the progressive loss of control of movements, muscle rigidity, poor balance, and disabling tremors. These symptoms result from the decrease in the amounts of dopamine in the brain that occurs due to the death of specialized dopamine-producing cells in the brain. In patients who suffer from Parkinson's

disease, by the time the disease becomes clinically apparent, about 80% of the cells associated with the production of dopamine are estimated to have died or have degenerated by a mechanism that is not yet understood. As these cells continue to die, the signs and symptoms of the disease become more difficult to manage, and the quality of life becomes severely compromised.

Unmet Medical Need

Levodopa is the primary approved treatment for early-stage Parkinson's disease. Levodopa can be converted into dopamine in the brain by an enzyme called AADC, and has been demonstrated to restore critical dopamine levels. However, as the disease progresses, levodopa tends to become less effective. This is believed to be due to the decline in concentrations of AADC that occur with continued neurodegeneration and cell death. Using higher levodopa doses in an attempt to compensate for less efficient conversion to dopamine often leads to intolerable side effects or toxicity.

AV201

We designed AV201 to restore and extend the therapeutic effectiveness of levodopa as a therapy for Parkinson's disease. AV201 is an AAV vector containing the gene for human AADC which is delivered directly to a patient's striatum, a part of the brain that requires dopamine to control movement which is not damaged by the disease. Patients with advanced Parkinson's disease receiving AV201 are expected to respond more readily to levodopa as the enhanced AADC expression should improve dopamine generation in the striatum, the principal target tissue.

We believe that the design of AV201 to work with the orally-administered levodopa is appealing in that it provides an added safety dimension by allowing patients' physicians to manage the therapeutic effect of the drug by regulating the amount of levodopa administered. In addition, using a technique known as FMT-PET, physicians may be able to monitor non-invasively the activity of AADC in the patient's brain during treatment.

Market for Parkinson's Disease Treatment

Parkinson's disease affects an estimated 2 million people in the U.S. and Europe according to prevalence rates from epidemiologic studies and World Health Organization population data. Based on information obtained from industry reports, we believe that the current amount spent on drugs to treat Parkinson's disease worldwide is approximately $1.8 billion per year, of which approximately 30% of this market represents sales of levodopa in various formulations. The cost of the disease increases as it progresses, both due to the need for increasing doses of therapeutic drugs, and because of an increasing need for assistance in performing activities of daily living. In 1999, a French study reported that drug costs were estimated to represent only 22% of the total costs for patients with Parkinson's disease, and that half of the patients in the study reported requiring help to perform daily living activities.

Preclinical Studies

We believe AV201 has shown considerable promise as a treatment in animal models of Parkinson's disease. We have demonstrated long-term expression of AADC for up to five years after a single administration of the gene, along with continued therapeutic benefit.

When treated with AV201, our rodent and primate models have displayed:

- a dose dependent increase in AADC activity as measured by PET;
- safe and quantitative delivery of the AADC gene to the striatum; and
- improved levodopa responses in rats and levodopa dose-reduction with retained clinical benefit in Parkinsonian monkeys.

Primates that were treated more than four years ago continue to show constant levels of AADC production as measured by PET and a decrease in Parkinsonian disease characteristics. The results in these and other animal models have encouraged us to pursue clinical treatment in humans. However, the observed successes of AV201 in animal models do not mean that we will be able to obtain the same results in humans. For example, we observed positive results in dog and mice models for the treatment of hemophilia B, but have so far been unable to replicate

these successes in humans. See "Risk Factors—The success of our current gene delivery technologies in animal models does not guarantee that the same results will be replicated in humans" below.

Clinical Trial

In August 2004, we received authorization from the FDA to initiate a phase I/II clinical trial of AV201, and in December 2004, we enrolled and treated our first subject. Our ongoing monitoring of the subject suggests that the procedure was well tolerated.

We have reviewed the results of our initial subject treatment with the FDA and have received clearance to accelerate the enrollment interval for subjects in dose level one of our AV201 clinical trial. Thus this study is open to enrollment and we are presently recruiting additional subjects.

Chronic Neuropathic Pain

The Disease

Pain is generally classified into two categories: nociceptive pain, which describes an acute, localized pain in response to an injury to the body, and neuropathic pain. Neuropathic pain is associated with damage or other insult to a nerve and often spreads to other areas of the body. Neuropathic pain can persist for a long time after the initial injury.

Neuropathic pain can be caused by many different insults and diseases including cancer, nerve damage caused by diabetes or chemotherapeutic agents, amputation, and viral infections such as herpes zoster (which causes shingles) and HIV. Many of the diseases that can lead to neuropathic pain can induce a chronic pain condition, independent of the duration of the initial insult. Neuropathic pain can present an aching, burning or sharply cutting sensation. Patients have reported that simple tasks, such as putting on socks, can be excruciatingly painful and that normal tactile sensations, including a light breath, can cause a skin burning sensation. Severe, spontaneous pain, in the absence of any stimulus, is also commonly reported.

Unmet Medical Need

Despite a common understanding among researchers in the field of the pathophysiology and molecular biology of the condition, patients with neuropathic pain are under-served. Drugs therapies include gabapentin (Neurontin), lidocaine patch (Lidoderm), tramadol (Ultram), antiepileptics, and tricyclic antidepressants. These therapies are generally only effective in a segment of the patient population and often only provide partial relief. Other patients, with severe neuropathic pain, may rely on oral or injected opioids such as morphine for pain relief. Unfortunately, these opioid therapies typically require substantial dose increases over time, and patients often must endure side effects including sedation, cognitive impairment, severe constipation, itching and edema. Addiction and the stigma of using narcotics are also major concerns for both patients and treating physicians.

AV333

AV333 represents an innovative approach to the treatment of unremitting pain, with demonstrated success in reversing neuropathic pain in established preclinical models. Traditionally, the development of treatments for neuropathic pain has focused on drugs that interact directly with neural cells. However, it is becoming more generally accepted that that neurons are not solely responsible for promoting and maintaining the pain state, and our understanding of their role in the central nervous system cannot adequately explain several types of observed pain states such as:

- pain in the absence of direct nerve injury such as a viral infection;
- extra-territorial pain or pain distant from any insult to a nerve;
- mirror-image pain or pain that is perceived not only in the affected tissue, but also in the corresponding part of the healthy side of the body; and
- phantom limb pain or pain located in an appendage that no longer exists due to amputation.

Mounting research suggests that other cells in the nervous system, called glial cells, may hold the key to understanding and treating neuropathic pain.

AV333 is a non-viral DNA-based drug candidate designed to deliver the human gene for the cytokine interleukin-10 (IL-10) into the intrathecal space surrounding the spinal cord. IL-10 is a naturally occurring protein that has demonstrated powerful anti-inflammatory properties. We believe that AV333 has the potential to lead to the production of IL-10 which will lessen the inflammatory process that is promoting or maintaining the pain state. The anti-inflammatory effects of IL-10 have been widely tested as a treatment for several autoimmune diseases; however high doses coupled with a short circulating half life of the protein have impeded product development efforts. We believe that our approach with AV333, to deliver the gene with the potential to express the protein locally, may be able to circumvent the challenges of other approaches. Preclinical results to date support a target product profile which is characterized by safe, effective, and durable relief of neuropathic pain.

Market for Neuropathic Pain Treatment

According to the International Association for the Study of Pain and other sources, pain accounts for over 70 million office visits per year in the United States. An American Pain Society study in 1999 found that over 50% of individuals with chronic, non-cancer-related pain classify their pain as severe or very severe, and that fewer than half of these feel that their pain is adequately controlled by currently available medication. In 2002, sales of oral opioids, a commonly prescribed prescription for chronic pain, were estimated to exceed $2 billion. In both 2003 and 2004, sales of Gabapentin, which is prescribed for both moderate neuropathic pain and for epilepsy, were estimated to exceed $2.7 billion.

Preclinical Studies

The work performed at Avigen and with our collaborators at the University of Colorado and elsewhere, in multiple commonly used rodent models of neuropathic pain, has demonstrated that an intrathecal administration of IL-10-encoding DNA exhibits reversal of chronic symptoms for prolonged periods of two to six weeks. The potential of this unique approach has led to our ongoing research and development efforts to optimize AV333 for spinal administration for treatment of neuropathic pain. The success of our technology in animal models, however, does not mean that we will be able to obtain the same results in humans. As stated above, we observed positive results in dog and mice models for the treatment of hemophilia B, but have so far been unable to replicate these successes in humans. See "Risk Factors — The success of our current gene delivery technologies in animal models does not guar antee that the same results will be replicated in humans" below.

Hemophilia

In May 2004, we ended subject enrollment in our phase I clinical trial of Coagulin-B, for the treatment of hemophilia B. This decision was made based on our identification of certain scientific, regulatory, and clinical hurdles which be believe would require much more time and investment to resolve than previously expected. This decision was not based on any perceived safety or subject tolerance concerns. In fact, to date, none of the 15 subjects that have participated in our two hemophilia clinical trials have reported any serious side effects associated with their exposure to our product candidates. We will continue to perform long term follow up for the subjects who participated in our hemophilia programs.

As part of our decision to suspend the hemophilia B clinical trial, we shifted resources into our other product development candidates that were more closely aligned with our long-term strategic focus on serious and life threatening neurological disorders such as Parkinson's disease and chronic neuropathic pain. Later, in July 2004, in response to these changes, we reduced our workforce by approximately 36% to reduce costs and extend the life of our financial resources to support the ongoing development of our other programs.

Despite the suspension of our hemophilia B program, our efforts resulted in significant progress towards establishing a proof of principle that gene therapy for hemophilia and other serious conditions may ultimately demonstrate clinical benefit. In addition, hemophilic dogs treated with our AAV vectors in preclinical animal studies continue to show ongoing therapeutic benefit six years after they received the treatment. As a result, we are actively exploring avenues to realize a return on the value created over the years in terms of know-how, manufacturing, intellectual property and clinical expertise.

Research Programs

Neuropathic Pain

We have a small preclinical research effort underway involving traditional pharmaceutical approaches to expand upon our commitment to developing novel therapeutics for the treatment of neuropathic pain. One collaborative effort represents an extension of the positive results from our AV333 project to further improve the product profile. We intend to continue to pursue additional exploratory pharmacology research around opportunistic applications we discover for validated small molecule candidates.

AAV vectors

We believe our AAV vector technology has the potential to treat a broad array of diseases that could benefit from long-term gene expression of therapeutic proteins. To this end, we have taken steps to promote the use of our technology within the larger research community. Since 2000, we have allowed a third-party licensor to distribute reagent kits that make it possible for researchers to make limited amounts of AAV vectors using our proprietary technology. We continue to perform research in this area and have also chosen to participate directly with selective collaborators to employ our AAV production expertise by supplying AAV vectors for collaborative studies.

An adeno-associated virus can be described simply as DNA encapsulated or packaged in a protein shell. We believe that many of the natural properties of AAV offer the potential to be used as a pharmaceutical drug. We have developed processes that modify AAV by extracting the virus' natural DNA and replacing it with a therapeutic gene of interest to make AAV vectors. We believe that AAV vectors benefit from many of the natural characteristics of AAV, which may allow them to efficiently deliver genes to targeted cells within a patient where the genes can be used as a template to produce continuous levels of therapeutic protein.

Non-Viral DNA

Non-viral DNA is DNA that is not encapsulated or packaged in a protein shell. Non-viral DNA has also been shown to be very safe, but is less efficient than AAV vectors at delivering genes to cells. As a result, non-viral DNA produces lower observable levels of therapeutic protein for a shorter period of time. However, these differences make non-viral DNA a preferred vehicle for circumstances when only a small amount of protein is required for only a period of weeks or months. We continue to perform research in this area, particularly in connection with our AV333 program. We believe that non-viral DNA can continue to be readministered if longer expression is required.

AAV Vector Manufacturing

We believe our current manufacturing facility has the capacity to manufacture sufficient quantities of our AAV vectors, in compliance with current good manufacturing practices (cGMP), to support the research efforts and clinical trial needs of ourselves and our potential collaboration partners.

We believe that our proprietary manufacturing process for AAV vectors, known as DNA transfection, offers many advantages over other methods of making AAV:

- Helper virus free — no live human pathogenic virus (e.g., adenovirus or herpes virus) is used in the manufacturing process.
- High-titer — more vector production per cell than that of other manufacturing methods.
- Flexibility—allows us to develop new vectors quickly and easily.
- Scaleable — other helper viruses need not be produced for large scale manufacturing.

In addition, our proprietary processes support two methods for purifying AAV vectors, including the use of either density gradient centrifugation or chromatographic means. Density gradient centrifugation separates the virus by its density compared to that of other impurities. Density gradient centrifugation has limited scalability compared

to column chromatographic techniques; however, it offers several other advantages for early product development. Most significantly, it is more cost effective for the production of smaller quantities of AAV vectors and it allows us to purify multiple AAVs or serotypes which are closely related, but not identical, to a target clinical product.

Chromatographic purification separates the virus by its ability to bind to certain chemicals versus that of other impurities. As demand for higher quantities of AAV vectors is required for later stage preclinical and clinical development, the scalable potential of chromatographic techniques is highly beneficial and cost effective. Avigen has developed more recent proprietary chromatographic purification methods which we believe will allow us to efficiently purify commercial quantities of AAV vectors.

We have designed and constructed our manufacturing facilities to accommodate large-scale vector production, as well as to meet the requirements of government mandated policies for pharmaceutical manufacturing, known as cGMPs. All of our facilities and long-lived assets are located in the United States.

We obtain materials used in the manufacture of our clinical vector products from a number of suppliers, some of whom are our sole qualified source of these materials. We qualify the suppliers of our clinical materials according to cGMP regulations. If we were to lose access to critical materials from any of these sole-source suppliers, we would be required to obtain a new source of the materials. It could take us several months to qualify new suppliers before we would be able to use their materials in the manufacture of our clinical vector products; however, we believe that we would eventually be able to find a secondary source for all materials critical to our manufacturing process. As of December 31, 2004, we did not have any significant outstanding commitments or obligations for future purchases of materials.

We also use certain hazardous materials, chemicals, biological materials, and various radioactive compounds in our research and development activities, which make us subject to a number of environmental laws and regulations, including the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, and the Resource Conservation and Recovery Act. We do not believe that our current level of use of these controlled substances will require any material capital expenditures for environmental control facilities for the next few years. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal regulations, we could be held liable for any damages that result from accidental contamination or injury.

Research and Development Expenses

We incurred research and development expenses of approximately $19.3 million, $21.8 million and $24.8 million in fiscal 2004, 2003 and 2002, respectively. During these years, we did not receive any reimbursements from governmental or other research grants or any other third parties to offset our expenses. As of December 31, 2004, we were not a party to any collaborative agreements that have potential for reimbursement of any future research and development expenses by a third party.

Patents and Intellectual Property

Patents and other proprietary rights are important to our business. We seek to procure patent protection for our anticipated products, or obtain protection from the relevant patents owned by our licensors. Our intellectual property strategy is to file patent applications that protect our technology, inventions and improvements to our inventions that we consider commercially important to the development of our business. We also rely on a combination of trade secrets, know-how and licensing opportunities to develop and protect intellectual property rights pertaining to our products and technology.

As of March 1, 2005, we owned, co-owned, or held licenses to 43 issued U.S. patents and 53 pending U.S. patent applications, as well as 32 issued non-U.S. patents and 70 pending non-U.S. patent applications. These patents are primarily related to our gene delivery products and protect rights that relate to the formulation of specific AAV vectors, methods of vector production, methods of tissue administration, and treatment of specific disease indications using AAV vectors. All issued patents within our current portfolio are scheduled to expire in the U.S. between 2008 and 2020.

When we identify previously patented technologies that we believe are critical to the development and commercialization of our products, we seek to in-license such rights under the most favorable terms. Such licenses

normally last for the life of the underlying patent. Licenses typically require us to pay license fees and royalties based on the net sales of products that fall within the scope of the license. Some licenses require us to exercise our best efforts to achieve research, clinical, and commercial milestones and may require us to make additional payments upon the completion of such milestones. In some cases, we were required to issue shares of our common stock, or warrants to purchase shares of our common stock at some future period, as partial consideration upon initiation of the license. Our failure to achieve any required development milestones or to negotiate appropriate extensions of any of our license agreements or to make all required milestone and royalty payments when due, and the subsequent decision of any such institution to terminate such license, could have a material adverse effect on our financial position.

The exclusive and non-exclusive licenses that we feel are important to our future commercial interests in our gene delivery products are:

University of Florida. In November 1992, we entered into an agreement with the University of Florida for rights to certain patents related to AAV transduction vectors. The license is non-exclusive for the duration of the patent, or until approximately 2009.

The Children's Hospital of Philadelphia (CHOP). In May 1999, we entered into an agreement with CHOP for rights to certain patents related to vectors and methods for treating hemophilia B using recombinant AAV vectors. The license is exclusive for the duration of the patent, or until approximately 2017.

The Rockefeller University and Yale University. In September of 2002, we entered into an agreement with The Rockefeller University and Yale University for rights to certain patents related to the delivery of recombinant AAV vectors to the nervous system, and to the use of such vectors for ameliorating symptoms of central nervous system disorders. The license is non-exclusive for the duration of the last to expire patent, or until approximately 2018.

University of Colorado. In November, 2003, we entered into an agreement with the University of Colorado for rights to certain intellectual property related to the treatment of chronic pain. The license is exclusive for the duration of any issued patents embodying the licensed intellectual property, or until approximately 2023.

In 2004, in connection with our decision to suspend our hemophilia program, we notified *BTG International Ltd.* of our intent to terminate the exclusive license that we entered into with BTG in March 2000. This license provided us with access to intellectual property rights covering the factor IX gene in the field of *in vivo* viral human gene therapy products. Since this patent will expire in early 2008, we believe it would no longer be a critical value-added component if we should decide to move our Coagulin-B program forward.

When we are party to co-owned technologies, we often seek to acquire exclusive licenses to the shared rights of our co-owner to the technologies. Licenses to co-owned technologies related to our gene delivery products include:

Johns Hopkins University (JHU). In September 1999, we entered into an agreement with JHU granting Avigen an exclusive license to JHU's rights in co-owned patents related to administration methods using AAV vectors and delivery methods for providing a therapeutic effect in any cardiomyopathy. The methods covered by this license include skeletal, smooth, and cardiac muscle, as well as delivery to the bloodstream, including intravenous and intra-arterial injection. This license excludes use to such methods to treat Pompe disease and alpha-1-antitrypsin. The license is for the duration of the underlying patents, or until approximately 2016.

Lawrence Berkeley National Laboratory (LBL). In July 2001, we entered into an agreement with LBL granting Avigen an exclusive license to LBL's rights in co-owned patents related to the treatment of Parkinson's disease. The license is for the duration of the last to expire patent, or until approximately 2018.

In consideration for each of the licenses listed above, we paid an initial license fee and are required to pay the licensor royalties based on net sales of future products that utilize the licensed technology. In connection with the licenses to the University of Colorado and BTG, we also issued warrants to purchase shares of our common stock at strike prices equal to the fair market value of our common stock on the respective effective date of each license agreement.

Our gene delivery programs currently involve our investigation and use of certain gene sequences or proteins encoded by those sequences, including certain forms of the IL-10 gene, and manufacturing processes that may be

or become patented by others, for which we do not currently own patent rights. As a result, we may be required to obtain licenses to these known gene sequences or proteins or other technology in order to continue to test, use or market related gene delivery products. However, we may not be able to obtain these licenses on terms favorable to us, if at all.

Legal standards relating to the validity and scope of claims in the biotechnology and biopharmaceutical fields are still evolving. As a result, our patent position is generally uncertain and involves complex legal and factual questions. In addition, since patent applications in the U.S. are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature often lags behind the actual discoveries, we cannot be certain that we or our licensors were first to make the inventions described in such patent applications. Accordingly, the degree of future protection for our patent rights is uncertain.

Competition

Pharmaceutical drug development is a highly competitive arena. We intend to pursue aggressively the acquisition or in-licensing of later-stage clinical development products in order to restructure and broaden our current portfolio. However, we expect to face intense competition in achieving this goal. Many of the companies and institutions that we will compete with to acquire later-stage development products have substantially greater capital resources, research and development staffs and facilities than we have, and substantially greater experience in conducting business development activities.

In addition to the later-stage development products we may acquire access to, other companies are developing treatments, including other compounds in various stages of preclinical and clinical development, which could target the same neurological indications in which we have interest. These companies are likely to include both public and private entities, including well-known, large pharmaceutical companies, chemical companies, biotechnology companies and research institutions.

For our gene delivery programs, the arena of gene therapy drug development continues to be a new and rapidly evolving field that is expected to continue to undergo significant and rapid technological change. We expect that these programs will experience intense competition from products from other companies in the gene therapy field, as well as companies that have other forms of treatment for the diseases being targeted. Ultimately, we believe that if we do develop gene delivery products that receive regulatory approval for commercialization, we will compete primarily on the basis of the efficacy of the treatment with the products.

We are aware of several development-stage and established enterprises, including major pharmaceutical and biotechnology firms that are exploring gene-based drugs or are actively engaged in gene delivery research and development. These include Cell Genesys, Inc., Corautus Genetics, Inc., GenVec, Inc., GlaxoSmithKline plc, and Targeted Genetics Corporation.

Our products for neurological diseases will face competition from both branded pharmaceuticals and generic compounds. Therapies for advanced Parkinson's disease are marketed by companies including GlaxoSmithKline, Pfizer Inc., Boehringer-Ingelheim GmbH, and Medtronic Inc. We are also aware of products for Parkinson's disease currently in development at both pharmaceutical and biotechnology firms including Schering-Plough Corporation, Schwartz Pharma AG, NeuroSearch A/S, Ceregene Inc., and Juvantia Pharma Ltd. Therapies for chronic pain range from over-the-counter compounds, such as aspirin, to opioids, such as morphine. Companies with compounds previously used off-label such as the anti-epileptic Neurontin (gabapentin, Pfizer), have performed clinical studies that support expansion of the label to include the treatment of pain. We are aware of additional compounds for chronic pain that are currently in development at numerous companies including Bayer, GlaxoSmithKline, Merck & Co., Inc., Novartis AG, Pfizer, Cognetix, Inc., GW Pharmaceuticals plc, Indevus Pharmaceuticals, Inc., Nastech Pharmaceutical Company Inc., Renovis, Inc., and Pain Therapeutics, Inc.

Companies that complete clinical trials, obtain required regulatory approvals, and commence commercial sales of their products before their competitors, may achieve a significant competitive advantage. In order to compete successfully, we must develop proprietary positions in patented products for therapeutic markets that have not been satisfactorily addressed by current alternatives for both our compound-based and gene-delivery products. These products, even if successfully tested and developed, may not be adopted by physicians over other products and may not offer economically feasible alternatives to other therapies.

Marketing and Sales

When feasible, we intend to retain rights to commercialize our products in the U.S. and expect to build marketing and sales capabilities using our own resources. However, we currently do not have a marketing or sales staff. If we are successful in achieving FDA approval of any product candidate that we may acquire as a result of our business development efforts, we will need to build a commercial capability. There is no assurance that we will be able to build our own commercial organization with our current resources.

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements on the clinical development, manufacture, distribution and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, distribution, record keeping, approval and promotion of our products. All of our products will require regulatory approval before commercialization. In particular, therapeutic products for human use are subject to rigorous preclinical and clinical testing and other requirements of the Federal Food, Drug, and Cosmetic Act, implemented by the FDA, as well as similar statutory and regulatory requirements of foreign countries and supervisory review boards affiliated with institutions that may perform our clinical trials.

Obtaining marketing approvals and subsequently complying with ongoing statutory and regulatory requirements is costly and time consuming. Any failure by us or our collaborators, licensors or licensees to obtain, or any delay in obtaining regulatory approval or in complying with other requirements, could adversely affect the commercialization of products then being developed by us and our ability to receive product or royalty revenues.

This process can take a number of years and typically requires substantial financial resources. The results of preclinical studies and initial clinical trials are not necessarily predictive of the results from large-scale clinical trials, and all clinical trials may be subject to additional costs, delays or modifications due to a number of factors, including the difficulty in obtaining enough subjects, clinical investigators, drug supply, or financial support, or because of unforeseen adverse effects. In addition, as a condition of approval, the FDA also can require further testing of the product and monitoring of the effect of commercialized products, and the agency has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Upon approval, a drug product may be marketed only in those dosage forms and for those indications approved in the new drug.

We believe that our proposed gene delivery products will be regulated as biologics by the FDA and comparable foreign regulatory bodies. Gene therapy is a relatively new technology and has not been extensively tested in humans. The regulatory requirements governing gene therapy products are uncertain and are subject to change. No gene therapy products have been approved to date in the U.S. Product development and approval within this regulatory framework can be unpredictable and may result in considerable time and expense to us.

Our decision to strategically restructure our portfolio of product candidates away from our historically funded gene delivery programs reflects our efforts to reduce our exposure to the regulatory review uncertainties we perceive are associated with gene therapy, and pursue more traditional product candidates that target life-threatening or chronic diseases with a risk-benefit profile that favors a more predictable and more accelerated traditional product development timeline.

In addition to obtaining FDA approval for each indication to be treated with each product, each domestic drug product manufacturing establishment must register with the FDA, list its drug products with the FDA, comply with current Good Manufacturing Practices and pass inspections by the FDA. Manufacturers of biological products also must comply with FDA general biological product standards. Moreover, the submission of applications for marketing approval from the FDA may require additional time to complete manufacturing stability studies. Foreign establishments manufacturing drug products for distribution in the United States also must list their products with the FDA and comply with current Good Manufacturing Practices. They also are subject to periodic inspection by the FDA or by local authorities under agreement with the FDA. If we rely on strategic relationships with third-party manufacturers, with either U.S. of foreign manufacturing establishments, we may not be able to ensure effective compliance with these FDA requirements which could impact the timing and potential success of our commercialization of our potential products. Because our current manufacturing facilities are located in California,

we are also required to obtain a drug manufacturing license from the State of California for any of our products administered to humans, including products tested in clinical trials

Other Regulations

In addition to regulations enforced by the FDA, in the U.S. we are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other federal, state and local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals, biological materials, and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal regulations, we could be held liable for any damages that result from accidental contamination or injury and this liability could exceed our resources.

Our clinical trials may also involve subjects that reside outside of the U.S. which can involve subsequent monitoring of the subjects' responses at clinical sites outside the U.S. where other regulations apply.

Employees

As of March 1, 2005, Avigen had 60 full-time employees, including 18 with Ph.D. degrees and 4 with M.D. degrees. Approximately 44 employees are involved in our research and development activities, including research, preclinical development, process development, clinical affairs, regulatory affairs, clinical manufacturing, and quality assurance and quality control, and 16 employees are involved in general administration, finance, legal, and business development activities. We also rely on a number of temporary staff positions and third-party consultants to supplement our workforce. None of our employees are represented by a collective bargaining agreement nor have we ever experienced a work stoppage. We believe that our relationship with our employees is good.

Revenues

Our revenues in 2004, 2003 and 2002 were $2,195,000, $463,000 and $57,000, respectively. Of these amounts, $2,125,000 and $375,000 in 2004 and 2003, respectively, were from the $2.5 million payment received from Bayer Corporation in 2003 in connection with our collaboration on the development of Coagulin-B for the treatment of hemophilia B to the liver. Bayer Corporation is located in the United States.

Available Information and Website Address

Our website address is www.avigen.com; however, information found on our website is not incorporated by reference into this Annual Report on Form 10-K. We file electronically with the Securities and Exchange Commission our annual reports on Form 10-K, quarterly interim reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15 (d) of the Securities Exchange Act of 1934. We make available on or through our website, free of charge, copies of these reports as soon as reasonably practicable after we electronically file or furnish it to the SEC. You can also request copies of such documents by contacting our Investor Relations Department at (510) 748-7150 or sending an email to *ir@avigen.com.*

RISK FACTORS

This section briefly discusses certain risks that should be considered by stockholders and prospective investors in Avigen. Many of these risks are discussed in other contexts in other sections of this report.

Risks Related to Our Business

We expect to continue to operate at a loss and we may never achieve profitability

Since our inception in 1992, we have not been profitable, and we cannot be certain that we will ever achieve or sustain profitability. To date, we have been engaged in research and development activities and have not generated any revenues from product sales. As of December 31, 2004, we had an accumulated deficit of $156.6 million. Acquiring and developing new compounds will require significant additional business development activities and research and development activities, including preclinical testing and clinical trials, and regulatory approval. We

expect these activities, together with our general and administrative expenses, to result in operating losses for the foreseeable future. Our ability to achieve profitability will depend, in part, on our ability to successfully identify, acquire, complete development of proposed products, and obtain required regulatory approvals and manufacture and market our approved products directly or through business partners.

Our success depends on our ability to enhance our existing pipeline of product candidates through the in-license or other acquisition of later-stage clinical development candidates, and if our business development efforts are not successful, our ability to achieve profitability will depend on the successful development of our earlier stage gene delivery product candidates and our ability to finance the development of such product candidates.

Our current product portfolio consists of early stage gene delivery products. We intend to restructure and expand our current portfolio and pursue aggressively the in-license or the acquisition of products in later-stage clinical development, primarily with more conventional pharmaceutical candidates. If we are not successful in acquiring products in later-stage clinical development, then we will be dependent upon our ability to raise financing for, and the successful development and commercialization of, our current gene delivery product candidates. Many other large and small companies within the pharmaceutical and biotechnology industry seek to establish collaborative arrangements for product research and development, or otherwise acquire products in later-stage clinical development, in competition with us. We face additional competition from public and private research organizations, academic institutions and governmental agencies in establishing collaborative arrangements for products in later-stage clinical development. Many of the companies and institutions that compete against us have substantially greater capital resources, research and development staffs and facilities than we have, and substantially greater experience in conducting business development activities. These entities represent significant competition to us as we seek to expand our pipeline through the in-license or acquisition of compounds. Moreover, while it is not feasible to predict the actual cost of acquiring additional product candidates, that cost could be substantial and we may need to raise additional financing or issue additional equity securities, either of which may further dilute existing stockholders, in order to acquire new products.

If we are able to enhance our existing pipeline of product candidates through the in-license or other acquisition of later-stage clinical development candidates, we may expose ourselves to new risks that were not identified prior to negotiating the in-license or other acquisition agreement that may prevent us from successfully developing or commercializing our product candidates

Even if we are able to in-license or acquire potential products, we may fail to identify risks during our due diligence efforts, or new risks may arise later in the development process of our product candidates, that we may be unable to adequately address. If we are unable to address such previously unidentified risks in a timely manner, our business and results of operations will be harmed.

Our historic research and development activities have primarily focused on our gene delivery products, which raises uncertainty about our ability to develop and commercialize more conventional small molecule product candidates effectively.

Even if we are able to in-license or acquire more conventional small molecule product candidates, we have limited experience in developing or commercializing such products. If we are unable to develop any new products we in-license or acquire effectively, it would significantly reduce our ability to create commercial opportunities for such products.

Many potential competitors who have greater resources and experience than we do may develop products and technologies that make ours non-competitive or obsolete

There are many entities, both public and private, including well-known, large pharmaceutical companies, chemical companies, biotechnology companies and research institutions, engaged in developing pharmaceuticals for neurological applications similar to those that may be targeted by us. Developments by these or other entities may render the products that we acquire or develop non-competitive or obsolete. Furthermore, many of our competitors are more experienced than we are in drug development and commercialization, obtaining regulatory approvals, and product manufacturing and marketing. Accordingly, our competitors may succeed in obtaining regulatory approval for products more rapidly and more effectively than we do. Competitors may succeed in

developing products that are more effective and less costly than any that we develop and also may prove to be more successful in the manufacturing and marketing of products. Any product that we successfully acquire or develop and for which we gain regulatory approval must then compete for market acceptance and market share. Accordingly important competitive factors, in addition to completion of clinical testing and the receipt of regulatory approval, will include product efficacy, safety, timing and scope of regulatory approvals, availability of supply, marketing and sales capacity, reimbursement coverage, pricing and patent protection.

We are aware that other companies are conducting preclinical studies and clinical trials for conventional and gene therapy products that could compete with products we intend to acquire or develop. See "Item 1. Business — Competition" for a more detailed discussion of the competition we face.

The regulatory process is expensive, time consuming and uncertain and may prevent us from obtaining required approvals for the commercialization of our product candidates

Prior to marketing in the United States, any product developed by us must undergo rigorous preclinical testing and clinical trials as well as an extensive regulatory approval process implemented by the FDA. This process is lengthy, complex and expensive, and approval is never certain. Positive results from preclinical studies and early clinical trials do not ensure positive results will be demonstrated in clinical trials designed to permit application for regulatory approval.

Potential problems we may encounter in the implementation stages of our studies include the chance that we may not be able to conduct clinical trials at preferred sites, obtain sufficient test subjects or begin or successfully complete clinical trials in a timely fashion, if at all. Furthermore, the FDA may temporarily suspend clinical trials at any time if it believes the subjects participating in trials are being exposed to unacceptable health risks, if it finds deficiencies in the clinical trial process or conduct of the investigation, or to better analyze data surrounding any unexpected developments. For example, progress in our suspended Coagulin-B clinical trials had been interrupted twice to better analyze data from unexpected observations. These included the identification of vector fragments in the seminal fluid of two early subjects beyond an expected timeframe and the development reported in December 2002 of a temporary elevation in the levels of two liver enzymes in one subject treated with a higher dose.

Because of the risks and uncertainties in biopharmaceutical development, our products could take a significantly longer time to gain regulatory approval than we expect or may never gain FDA approval. If we do not receive these necessary approvals from the FDA, we will not be able to generate substantial revenues or become profitable.

We may not be successful in obtaining required foreign regulatory approvals, which would prevent us from marketing our products internationally

We cannot be certain that we will obtain any regulatory approvals in other countries. In order to market our products outside of the United States, we must comply with numerous and varying foreign regulatory requirements implemented by foreign regulatory authorities. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA approval. The foreign regulatory approval process includes all of the risks associated with obtaining FDA approval set forth above, and approval by the FDA does not ensure approval by the regulatory authorities of any other country.

If we fail to comply with regulatory requirements, or if we experience unanticipated problems with our approved products, our products could be subject to restrictions or withdrawal from the market.

Any product for which we obtain marketing approval from the FDA, along with the manufacturing processes, post-approval clinical data collection and promotional activities for such product, will be subject to continual review and periodic inspection by the FDA and other regulatory bodies. After approval of a product, we will have significant ongoing regulatory compliance obligations. Later discovery of previously unknown problems with our products or manufacturing processes, or failure to comply with regulatory requirements, may result in penalties or other actions, including removal from the market.

We may need to secure additional financing to acquire and complete the development and commercialization of our products

We anticipate that our existing capital resources as of December 31, 2004 will be adequate to fund our needs for at least the next three to four years. However, beyond that we may require additional funding to acquire new

products, to complete the research and development activities currently contemplated, and to commercialize our products. Our future capital requirements will depend on many factors, including:

- how successful, if at all, we are at in-licensing compounds, and the nature of the consideration we pay for in-licensing compounds;
- continued scientific progress in research and development programs;
- the scope and results of preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing, prosecuting and enforcing patent claims and other intellectual property rights;
- the costs involved in obtaining licenses to patented technologies from third-parties that may be needed to commercialize our products;
- competing technological developments;
- the cost of manufacturing scale-up;
- the cost of commercialization activities; and
- other factors which may not be within our control.

We intend to continue to seek additional funding through public or private equity or debt financing, when market conditions allow, or through additional collaborative arrangements with corporate partners. If we raise additional funds by issuing equity securities there may be further dilution to existing stockholders. We cannot assure our investors that we will be able to enter into such financing arrangements on acceptable terms or at all. Without such additional funding, we may be required to delay, reduce the scope of, or eliminate one or more of our research or development programs.

We have limited experience in manufacturing potential products we may acquire and may in the future depend on third parties to manufacture our products. If these manufacturers fail to meet our requirements and the requirements of regulatory authorities, our business, financial condition and results of operations could be harmed

We may not have the internal capability to manufacture commercial quantities of the pharmaceutical products we acquire following the FDA's regulations concerning current good manufacturing practices (cGMP). In order to continue to develop products, apply for regulatory approvals and commercialize our products, we may need to contract for or otherwise arrange for the necessary manufacturing capabilities. If we are unable to enter into supply and processing contracts with any of these manufacturers or processors, there may be additional costs and delay in the development and commercialization of our products. Even if we are able to enter into supply and processing contracts with any of these manufacturers or processors, such manufacturers or processors may be unable to satisfy our requirements, which may lead to additional cost and delay in the development or commercialization of our products. If we are required to find an additional or alternative source of supply, there may be additional cost and delay in the development or commercialization of our products. Additionally, the FDA inspects all commercial manufacturing facilities before approving a New Drug Application for a drug manufactured at those sites. If any of our manufacturers or processors fails to pass this the FDA inspection, the approval and eventual commercialization of our products may be delayed.

If our product manufacturers fail to comply with regulatory requirements, our product commercialization could be delayed or subject to restrictions.

Any contract manufacturers that we use must adhere to the FDA's regulations on cGMP, which are enforced by the FDA through its facilities inspection program. These facilities must pass a plant inspection before the FDA will issue an approval of the product. The manufacture of product at these facilities will be subject to strict quality control, testing and recordkeeping requirements. Moreover, while we may choose to manufacture our products in the future, we have limited experience in the manufacture of pharmaceutical products for clinical trials or commercial purposes. If we decide to manufacture products, we would be subject to the regulatory requirements

described above. In addition, we may require substantial additional capital and would be subject to delays or difficulties encountered in manufacturing pharmaceutical products.

No matter who manufactures the product, we will be subject to continuing obligations regarding the submission of safety reports and other post-market information. If we encounter delays or difficulties with contract manufacturers, packagers or distributors, market introduction and subsequent sales of our products could be delayed. If we change the source or location of supply or modify the manufacturing process, regulatory authorities will require us to demonstrate that the product produced by the new source or from the modified process is equivalent to the product used in any clinical trials that were conducted. If we are unable to demonstrate this equivalence, we will be unable to manufacture products from the new source or location of supply, or use the modified process, we may incur substantial expenses in order to ensure equivalence, and it may harm our ability to generate revenues.

We have limited experience in manufacturing our potential gene delivery products at a commercial scale, which raises uncertainty about our ability to manufacture our potential products cost-effectively

Even if we are able to develop our potential gene delivery products and obtain necessary regulatory approvals, we have limited experience in manufacturing any of our proposed products on a commercial basis. If we are unable to manufacture our products in a cost-effective manner, we are not likely to become profitable. We have not yet received a license from the FDA for our manufacturing facilities, and cannot apply for one until we submit our product for commercial approval. Even if we do receive a manufacturing license, we may fail to maintain adequate compliance with the FDA's cGMP, in which case the license, and our authorization to manufacture product, could be revoked.

We, or our manufacturers, may lose access to critical materials from single source suppliers, which is not within our control and could delay us from manufacturing materials needed to support our clinical trials or future commercialization

We, and any manufacturers with whom we may contract, may be required to obtain materials used in the manufacture of our clinical products from suppliers, some of whom could be the sole qualified source of these materials. These suppliers of our clinical materials must be qualified according to cGMP regulations. If these sources are unable or unwilling to provide critical materials to us, or our manufacturers, in required quantities or on acceptable terms, we would likely incur significant costs and delays in order to identify and qualify a new source of the materials. It could take us several months to qualify new suppliers before we could use their materials in the manufacture of our clinical products.

If we are able to bring our potential products to market, we continue to face a number of risks including our inexperience in marketing or selling our potential products, the acceptance of our products by physicians and insurers, our ability to price our products effectively and to obtain adequate reimbursement for sales of our products.

Even if we are able to develop our potential products and obtain necessary regulatory approvals, we have no experience in marketing or selling any of our proposed products. We currently do not have a marketing or sales staff. If we are successful in achieving FDA approval of any product candidate, including any product that we may acquire as a result of our business development efforts, we will need to build a commercial capability. The development of a marketing and sales capability will require significant expenditures, management resources and time. We may be unable to build such a sales force, the cost of establishing such a sales force may exceed any product revenues, or our marketing and sales efforts may be unsuccessful. We may not be able to find a suitable sales and marketing partner for our products. If we are unable to successfully establish a sales and marketing capability in a timely manner or find suitable sales and marketing partners, our business and results of operations will be harmed. Even if we are able to develop a sales force or find a suitable marketing partner, we may not successfully penetrate the markets for any of our proposed products.

We intend to enter into distribution and marketing agreements with other companies for our products outside the U.S. and do not anticipate establishing our own foreign sales and marketing capabilities for any of our potential products in the foreseeable future. If any of our foreign marketing partners do not perform under future agreements, we would need to identify an alternative marketing and distribution partner, or market this product ourselves, and we may not be able to establish adequate marketing capabilities for this product.

Our success is dependent on acceptance of our products. We cannot assure you that our products will achieve significant market acceptance among patients, physicians or third-party payers, even if we obtain necessary regulatory and reimbursement approvals. Failure to achieve significant market acceptance will harm our business. In addition, we cannot assure you that these products will be considered cost-effective and that reimbursement to the consumer will be available or will be sufficient to allow us to sell our products on a profitable basis. In both the United States and elsewhere, sales of medical products and treatments are dependent, in part, on the availability of reimbursement to the consumer from third-party payers, such as government and private insurance plans. Third-party payers are increasingly challenging the prices charged for medical products and services. We cannot predict whether any legislative or regulatory proposals will be adopted or the effect that such potential proposals or managed care efforts may have on our business.

We may be unable to attract and retain the qualified employees, consultants and advisors we need to be successful

We are highly dependent on key members of our senior management and scientific staff. The loss of any of these persons could substantially impair our research and development efforts and impede our ability to develop and commercialize any of our products. Recruiting and retaining qualified scientific, technical and managerial personnel will also be critical to our success. Biotechnology and pharmaceutical personnel with these skills are in high demand. As a result, competition for and retention of personnel, particularly for employees with technical expertise, is intense and the turnover rate for these people can be high.

In addition, we rely on consultants and advisors to assist us in formulating our research and development strategy. A majority of our scientific advisors are engaged by us on a consulting basis and are employed on a full-time basis by others. We have limited control over the activities of these scientific collaborators which often limit their availability to us. Failure of any of these persons to devote sufficient time and resources to our programs could delay our progress and harm our business. In addition, some of these collaborators may have consulting or other advisory arrangements with other entities that may conflict or compete with their obligations to us.

We face the risk of liability claims which may exceed the scope or amount of our insurance coverage

The manufacture and sale of medical products entail significant risk of liability claims. We currently carry liability insurance; however, we cannot assure you that this coverage will remain in place or that this coverage will be adequate to protect us from all liabilities which we might incur in connection with the use of our products in clinical trials or the future use or sale of our products upon commercialization. In addition, we may require increased liability coverage as additional products are used in clinical trials and commercialized. This insurance is expensive and may not be available on acceptable terms in the future, if at all. A successful liability claim or series of claims brought against us in excess of our insurance coverage could harm our business. We must indemnify certain of our licensors against any liability claims brought against them arising out of products developed by us under these licenses.

Our use of hazardous materials exposes us to the risk of environmental liabilities, and we may incur substantial additional costs to comply with environmental laws in connection with the operation of our research and manufacturing facilities

We use radioactive materials and other hazardous substances in our research and development and manufacturing operations. As a result, we are potentially subject to substantial liabilities related to personal injuries or property damages they may cause. In addition, clean up costs associated with radioactivity or other hazardous substances, and related damages or liabilities could be significant and could harm our business. We are required to comply with increasingly stringent laws and regulations governing environmental protection and workplace safety which could impose substantial fines and criminal sanctions for violations. Maintaining compliance with these laws and regulations could require substantial additional capital.

Risks Related to Our Current Gene Delivery Products

Our clinical trial to date for AV201 for the treatment of Parkinson's disease has only treated one subject over a short period of time, and the results we observe may not be indicative of future results in a larger number of subjects or have lasting effects

Our current Parkinson's disease clinical trial has only treated one subject and any observed progress or results may not be indicative of subsequent progress or results achieved from larger populations. At this early stage of

our AV201 clinical trial, we do not yet know if we will achieve any favorable results, or if any favorable results achieved will have a lasting effect. Further, in our previous clinical trials for hemophilia, we experienced difficulties in obtaining positive results in humans reflective of positive results we obtained in animal models. If a larger population of subjects does not experience positive results, or if any favorable results that we achieve do not demonstrate a lasting effect, this product candidate may not receive approval from the FDA for further studies or commercialization. If we are not able to proceed with, or decide to abandon our AV201 development program, our business prospects may be impaired.

The success of our current gene delivery technologies in animal models does not guarantee that the same results will be replicated in humans

Even though our current product candidates have shown successful results in mouse, dog, and non-human primate models, animals are different than humans and results in animal models may not be replicated in our clinical trials with humans. For example, while the results of our gene therapy treatment for hemophilia B were favorable and demonstrated sustained long-term expression in both dogs and mice for multiple years, one human subject who demonstrated therapeutic levels of circulating factor IX when given a comparable dose size to that used in the successful animal studies was not able to sustain steady factor IX expression beyond five weeks. In addition, this human subject experienced a mild, temporary elevation of two liver enzymes, which was not seen in any of the animal models. Further, we experienced an immune system response to our hemophilia product candidate that we did not observe in the animal models, which we have not yet been able to, and may not be able to, adequately address. Consequently, you should not rely on the results in any of our animal models as being predictive of the results that we will see in our clinical trials with humans.

Adverse events in the field of gene therapy may negatively impact regulatory approval or public perception of our potential gene delivery products

The commercial success of our potential gene delivery products will depend in part on public acceptance of the use of gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy is unsafe, and consequently our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements for gene therapy products, including any of our products, and could cause a decrease in the demand for any products we may develop.

Our stock price is also influenced by public perception. For example, in January 2003, a report of serious adverse events in a retroviral trial for infants diagnosed with severe combined immunodeficiency (SCID) in France and subsequent FDA actions putting related trials on hold in the United States had a significant impact on the public perception and stock price of all companies involved in gene therapy. Our stock declined despite the fact that we do not work with retroviruses or with infants diagnosed with SCID and our clinical trial was not affected by the FDA's actions in this case.

Other potential adverse events in the field of gene therapy may occur in the future that could result in greater governmental regulation of our potential products and potential regulatory delays relating to the testing or approval of our potential products.

AAV technology is new and developing rapidly; there is limited clinical data and new information may arise which may cause delays in designing our protocols, submitting applications that satisfy all necessary regulatory review requirements, and ultimately completing the clinical trials of our products

Clinical trials are governed by regulations enforced by the FDA. Our technology is fairly new, and we have limited historical data from preclinical studies or clinical trials that are often necessary to satisfy the FDA's regulatory review process. In addition, as new information about the technology becomes available, it may change perceptions of previously accepted data, which could require additional periods of time to review and interpret these data. For example, we experienced what appears to be an immune system response to our hemophilia product candidate that was not previously seen in, and we have not yet been able to reproduce in, any animal model and which we have not yet been able to, and may not be able to, adequately address. Further clinical testing is required to confirm to what extent our product candidates might cause human patients to develop immune responses to these

potential products or the proteins produced by these potential products. Such responses could make our product ineffective or lead to unwanted side effects. In addition, as previously discussed, one human subject in our clinical trial experienced a mild, temporary elevation of two liver enzymes, which was not seen in any of the animal models, and was not able to sustain steady factor IX expression beyond five weeks. Consequently, we may encounter deficiencies in the design or application stages while developing our clinical trial studies, or in the subsequent implementation stages of such studies, which could cause us or the FDA to delay, suspend or terminate our trials at any time.

Because our gene delivery product candidates are in an early state of development, there is a high risk that they may never be commercialized

All of our product candidates are in early stages of development. We do not have any product candidates that have received regulatory approval for commercial sale, and we face the risk that none of our product candidates will ever receive regulatory approval. We have one product candidate in clinical trials, AV201 for the treatment of Parkinson's disease. This product candidate is only in phase I/II of the clinical trial process. We are not aware of any other gene therapy products of other companies that have received regulatory approval for commercial sale in the U.S., and do not expect any of our prospective products, including AV201, to be commercially available for at least several years. As results of our clinical trial become available and are evaluated, we may decide at any time to discontinue any further development of one or more of our product candidates.

The testing of our potential products relies heavily on the voluntary participation of subjects in our clinical trials, which is not within our control, and could substantially delay or prevent us from completing development of such products

The development of our potential products is dependent upon collecting sufficient data from human clinical trials to demonstrate safe and effective results. We experienced delays in enrolling subjects in our now suspended clinical trials for hemophilia B, and we may experience similar difficulties in the future. Any delay or failure to recruit sufficient numbers of subjects to satisfy the level of data required to be collected under our clinical trial protocols could prevent us from developing any products we may target.

Risks Related to Our Intellectual Property

Our success is dependent upon our ability to effectively protect our patents and proprietary rights, which we may not be able to do

Our success will depend to a significant degree on our ability to obtain patents and licenses to patent rights, preserve trade secrets, and to operate without infringing on the proprietary rights of others. If we are not successful in these endeavors, our business will be substantially impaired.

To date, we have filed a number of patent applications in the U.S. relating to technologies we have developed or co-developed. In addition, we have acquired exclusive and non-exclusive licenses to certain issued patents and pending patent applications. We cannot guarantee that patents will issue from these applications or that any patent will issue on technology arising from additional research or, if patents do issue, that claims allowed will be sufficient to protect our technologies.

The patent application process takes several years and entails considerable expense. The failure to obtain patent protection on the technologies underlying our proposed products may have a material adverse effect on our competitive position and business prospects. Important legal issues remain to be resolved as to the scope of patent protection for biotechnology products, and we expect that administrative proceedings, litigation, or both may be necessary to determine the validity and scope of our and others' biotechnology patents. These proceedings or litigation may require a significant commitment of our resources in the future.

If patents can be obtained, we cannot assure you that any of these patents will provide us with any competitive advantage. For example, others may independently develop similar technologies or duplicate any technology developed by us, and patents may be invalidated or held unenforceable in litigation.

In addition, several of our patents and patent applications are co-owned with co-inventors or institutions. To date, we have negotiated exclusive licenses for many of our co-owned technologies. However, if we cannot negotiate

exclusive rights to other co-owned technology, each co-inventor may have rights to independently make, use, and offer to sell or sell the patented technology. Commercialization, assignment or licensing of the technology by a co-owner could harm our business.

We also rely on a combination of trade secret and copyright laws, employee and third-party nondisclosure agreements and other protective measures to protect intellectual property rights pertaining to our products and technologies. We cannot be certain that these measures will provide meaningful protection of our trade secrets, know-how or other proprietary information. In addition, the laws of certain foreign countries do not protect our intellectual property rights to the same extent as do the laws of the United States. We cannot assure you that we will be able to protect our intellectual property successfully.

Other persons may assert rights to our proprietary technology, which could be costly to contest or settle

Third parties may assert patent or other intellectual property infringement claims against us with respect to our products, technologies, or other matters. Any claims against us, with or without merit, as well as claims initiated by us against third parties, can be time-consuming and expensive to defend or prosecute and resolve. There may be third-party patents and other intellectual property relevant to our products and technology which are not known to us. We have not been accused of infringing any third party's patent rights or other intellectual property, but we cannot assure you that litigation asserting claims will not be initiated, that we would prevail in any litigation, or that we would be able to obtain any necessary licenses on reasonable terms, if at all. If our competitors prepare and file patent applications in the U.S. that claim technology also claimed by us, we may have to participate in interference proceedings declared by the Patent and Trademark Office to determine priority of invention, which could result in substantial cost to us, even if the outcome is favorable to us. In addition, to the extent outside collaborators apply technological information developed independently by them or by others to our product development programs or apply our technologies to other projects, disputes may arise as to the ownership of proprietary rights to these technologies.

We may be required to obtain rights to proprietary genes and other technologies to further develop our business, which may not be available or may be costly

We currently investigate and use certain gene sequences or proteins encoded by those sequences, including the IL-10 gene, and manufacturing processes that are or may become patented by others. As a result, we may be required to obtain licenses to these gene sequences or proteins or other technology in order to test, use or market products. We may not be able to obtain these licenses on terms favorable to us, if at all. In connection with our efforts to obtain rights to these gene sequences or proteins or other technology, we may find it necessary to convey rights to our technology to others. Some of our products may require the use of multiple proprietary technologies. Consequently, we may be required to make cumulative royalty payments to several third parties. These cumulative royalties could become commercially prohibitive. We may not be able to successfully negotiate these royalty adjustments to a cost effective level, if at all.

If we do not achieve certain milestones, we may not be able to retain certain licenses to our intellectual property

We have entered into license agreements with third parties for technologies related to our gene delivery product development programs. Some of these license agreements provide for the achievement of development milestones. If we fail to achieve these milestones or to obtain extensions, the licensor may terminate these license agreements with relatively short notice to us. Termination of any of our license agreements could harm our business.

Risks Related to Our Stock

Anti-takeover effects of certain charter provisions and Delaware law may negatively affect the ability of a potential buyer to purchase some or all of our stock at an otherwise advantageous price, which may limit the price investors are willing to pay for our common stock

Certain provisions of our charter and Delaware law may negatively affect the ability of a potential buyer to attempt a takeover of Avigen, which may have a negative effect on the price investors are willing to pay for our common stock. For example, our board of directors has the authority to issue up to 5,000,000 shares of preferred

stock and to determine the price, rights, preferences, and privileges of those shares without any further vote or action by the stockholders. This would enable the Board of Directors to establish a shareholder rights plan, commonly referred to as a "poison pill," which would have the effect of making it more difficult for a third party to acquire a majority of the outstanding voting stock of Avigen. In addition, our board of directors is divided into three classes, and each year on a rotating basis the directors of one class are elected for a three-year term. This provision could have the effect of making it less likely that a third party would attempt to obtain control of Avigen through Board representation. Furthermore, certain other provisions of our restated certificate of incorporation may have the effect of delaying or preventing changes in control or management, which could adversely affect the market price of our common stock. In addition, we are subject to the provisions of Section 203 of the Delaware General Corporation Law, an anti-takeover law.

Our stock price is volatile, and as a result investing in our common stock is very risky

From January 1, 2003 to March 1, 2005, our stock price has fluctuated between a range of $2.75 and $7.93 per share. We believe that various factors may cause the market price of our common stock to continue to fluctuate, perhaps substantially, including announcements of:

- technological innovations or regulatory approvals;
- results of clinical trials;
- new products by us or our competitors;
- developments or disputes concerning patents or proprietary rights;
- achieving or failing to achieve certain developmental milestones;
- public concern as to the safety of gene therapy, recombinant biotechnology or traditional pharmaceutical products;
- health care or reimbursement policy changes by governments or insurance companies;
- developments in relationships with corporate partners; or
- a change in financial estimates or securities analysts' recommendations.

In addition, in recent years, the stock market in general, and the shares of biotechnology and health care companies in particular, have experienced extreme price fluctuations. These broad market and industry fluctuations may cause the market price of our common stock to decline dramatically.

Item 2. ***Properties***

We lease an aggregate of 112,500 square feet in two buildings located in a commercial neighborhood of Alameda, California for our manufacturing, research laboratory and office space. One building, which represents approximately 45,000 square feet, is under a 5-year lease that is scheduled to expire in July 2008. A second adjacent building, which represents approximately 67,500 square feet, is under a 10-year lease that is scheduled to expire in November 2010. We believe that these two buildings are more than adequate for our needs for the foreseeable future.

Item 3. ***Legal Proceedings***

As of March 1, 2005, we were not involved in any legal proceedings.

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

None.

Executive Officers of the Registrant

Our executive officers and their respective ages and positions as of March 11, 2005, are as follows:

Name	Age	Position
Philip J. Whitcome, Ph.D.	56	Chairman of the Board
Kenneth G. Chahine, J.D., Ph.D. ...	40	President, Chief Executive Officer and Director
Thomas J. Paulson	58	Vice President, Finance, Chief Financial Officer and Secretary
Glenn Pierce, Ph.D., M.D.	49	Vice President, Research and Clinical Development
Dawn McGuire, M.D.	51	Chief Medical Officer
Michael D. Coffee	59	Chief Business Officer
Kirk Johnson, Ph.D.	45	Vice President, Preclinical Research
M. Christina Thomson, J.D.	34	Vice President, Corporate Counsel

All of our officers are elected annually by the Board of Directors. There is no family relationship between or among any of the officers or directors.

Philip J. Whitcome, Ph.D., has served as a director of Avigen since December 1992. In April 1995, Dr. Whitcome was elected Chairman of the Board and from March 1996 to December 1996 he served as acting Chief Financial Officer. From 1988 to 1994, Dr. Whitcome was President and Chief Executive Officer of Neurogen Corporation, a biopharmaceutical company. From 1981 to 1988, Dr. Whitcome was employed at Amgen Inc., a biopharmaceutical company, including service as Director of Strategic Planning. Prior to joining Amgen, he served as Manager of Corporate Development for Medical Products at Bristol-Myers Squibb Company, a pharmaceutical and healthcare products company, and held research and marketing management positions with the Diagnostics Division of Abbott Laboratories, a pharmaceutical and medical products company. Dr. Whitcome holds a Ph.D. in Molecular Biology from the University of California at Los Angeles, an M.B.A. from the Wharton School at the University of Pennsylvania and a B.S. in Physics from Providence College.

Kenneth G. Chahine, J.D., Ph.D., was appointed President, Chief Executive Officer and director of Avigen in March 2004. Dr. Chahine joined Avigen in 1998, was appointed Vice President, Business Development in January 1999, and was appointed Chief Operating Officer in July 2002. Prior to joining Avigen, Dr. Chahine worked at the patent law firm of Madson & Metcalf, P.C. in Salt Lake City, Utah from 1994 to 1998. Between 1992 and 1993, Dr. Chahine worked as a research scientist at Parke-Davis Pharmaceuticals, a pharmaceutical company, and held another research scientist post at the University of Utah Department of Human Genetics from 1994 through 1996. Dr. Chahine also served as Western Regional News and Legal Correspondent for Nature Biotechnology from 1996 to 2002. Dr. Chahine holds a J.D. from the University of Utah and a Ph.D. in Biochemistry and Molecular Biology from the University of Michigan.

Thomas J. Paulson joined Avigen and was appointed Vice President, Finance, Chief Financial Officer and Secretary of Avigen effective September 20, 1996. Prior to joining Avigen, Mr. Paulson was president of Paulson Associates, a biotechnology consulting firm. From its inception in 1989 until 1994, Mr. Paulson was Chief Financial Officer of Neurogen Corporation, a pharmaceutical company. From 1986 to 1989, he was Director of Finance at Ciba-Corning Diagnostics, Gilford Systems, a diagnostics instrument company. From 1984 to 1986, Mr. Paulson served as financial director at Quidel Corporation, a biotechnology company. From 1971 to 1984, Mr. Paulson held various financial management positions at Abbott Laboratories, a pharmaceutical and medical products company. Mr. Paulson holds an M.B.A. from the University of Chicago Graduate School of Business and a B.B.A. in Accounting from Loyola University in Chicago.

Glenn Pierce, Ph.D., M.D., joined Avigen and was appointed Vice President, Research and Clinical Development in November 2002. Before joining Avigen, from 1998 to November 2002, Dr. Pierce was Vice President, Therapeutic Product Development at Selective Genetics, a gene therapy company he helped found, which focused on tissue regeneration. From 1994 to 1998, he served as Vice President, Preclinical Development at Prizm Pharmaceuticals, a pharmaceutical company. Prior to that, Dr. Pierce held a number of positions at Amgen Inc., a biopharmaceutical company, and was instrumental in the development of Amgen's neurobiology, tissue regeneration, and experimental pathology programs. Dr. Pierce holds numerous patents in various areas of drug delivery, tissue engineering, medical devices and viral vectors. He has published more than 100 papers in scientific and medical journals in related areas. He has served three terms as the president of the National Hemophilia

Foundation (NHF) and initiated the NHF's annual gene therapy workshop in 1996. He earned both his M.D. and a Ph.D. in Immunology and Experimental Pathology at Case Western Reserve University, prior to doing a pathology residency and hematology research fellowship at Washington University in St. Louis.

Dawn McGuire, M.D., has served as our Chief Medical Officer since January 2004. Dr. McGuire has provided leadership in both pharmaceutical and biotechnical corporate settings, most recently as Chief Scientific Officer of Eunoe, Incorporated (previously CSFluids, Inc.), a medical device company, from 2002 to January 2004. She was President and Chief Executive Officer of CSFluids from 1999 to 2002. From 1999 to 2000, Dr. McGuire also served as Vice President, Medical Affairs Worldwide at Collagen Corporation, a healthcare products company. From 1997 to 1999, Dr. McGuire served as Vice President, Clinical Research and Medical Affairs at Elan Pharmaceuticals and was responsible for, among other programs, the development through FDA submission of ziconotide (Prialt™). Dr. McGuire is a board-certified neurologist and has led clinical development programs in neuropathic pain, Alzheimer's disease, AIDS dementia, Lou Gehrig's disease, Multiple Sclerosis, and stroke. She is the co-author of over 40 scientific articles, book chapters and invited reviews in neurotherapeutics. Since 2000, Dr. McGuire has served as a Scientific Reviewer and Study Section Member of the National Institute of Neurological Disorders and Stroke. Dr. McGuire received her B.A. with high honors from Princeton University, her M.D. from Columbia University College of Physicians and Surgeons, and trained in Neurology at the University of California, San Francisco, followed by an NIH-funded postdoctoral fellowship in clinical trial design and experimental therapeutics.

Michael D. Coffee joined Avigen and was appointed Chief Business Officer in February 2005. In 2004, Mr. Coffee co-founded the Alekta Group, LLC, a consulting firm which provided a comprehensive range of pharmaceutical development advisory services to emerging pharmaceutical companies. From January 2001 to February 2004 he served as President and Chief Operating Officer of Amarin Pharmaceuticals Inc., the U.S. drug development and marketing subsidiary of Amarin Corporation plc. Mr. Coffee also served as President and Chief Operating Officer of Elan Pharmaceuticals, North America from August 1998 to January 2001 and held marketing and executive management positions, including President and Chief Operating Officer, of Athena Neurosciences, Inc. between 1991 and 1998. Mr. Coffee received a BS in Biology from Siena College.

Kirk Johnson, Ph.D., joined Avigen in January 2004 and was appointed Vice President, Preclinical Development in June 2004. Prior to joining Avigen, Dr. Johnson was Senior Director, Pharmacology & Preclinical Development and a member of the executive management team of Genesoft Pharmaceuticals from 2001 to 2004. From 1991 to 2001, Dr. Johnson was employed at Chiron Corporation, a biopharmaceutical company, and held various scientific research positions including Director, Pharmacology and Preclinical Research. His experience includes work with both protein and small molecule therapeutic research and development activities and he has been involved in leading IND-enabling programs, supporting clinical development, and in contributing to successful IND and NDA filings as well as product launch. In addition to general pharmacology and other preclinical development responsibilities, Dr. Johnson has lead research and clinical development projects for diverse indications including hemophilia, antibacterials, diabetes, obesity, acute inflammation and cardiovascular disease and has published approximately 50 manuscripts and holds 4 U.S. patents. Dr. Johnson earned a B.S. in Toxicology from U.C. Davis, a Ph.D. in Pharmacology and Toxicology from the Medical College of Virginia, and he trained in postdoctoral fellowships studying the mechanism of action of IL-2 from 1986-1989 with Dr. Kendall Smith at Dartmouth College and from 1990-1991 with Dr. Marian Koshland at the University of California, Berkeley.

M. Christina Thomson, J.D., joined Avigen in February 2000 and was appointed Vice President, Corporate Counsel in June 2004. She has also served as our Chief Compliance Officer since March 2004. Ms. Thomson is a registered patent attorney, and has managed the growth in Avigen's patent portfolio over the last five years from nine issued U.S. patents to 39. She also oversees the company's litigation and administrative patent proceedings, as well as contract administration. Prior to joining Avigen, Ms. Thomson worked as a patent attorney with the law firm Knobbe Martens Olson & Bear LLP in Newport Beach, California, a patent agent with Madson & Metcalf, P.C. in Salt Lake City, Utah, and a scientist for Myriad Genetic Laboratories. Ms. Thomson holds a J.D. from the University of Utah College of Law and an M.S. in Biology from the University of Utah.

PART II

Item 5. ***Market for Registrants Common Equity, Related Stockholder Matters, and Issuer Purchases of Equity Securities***

Shares of Avigen's common stock commenced trading on the NASDAQ National Market on May 22, 1996, under the symbol "AVGN". As of March 1, 2005, there were approximately 140 holders of record of our common stock.

We have never paid cash dividends and do not anticipate paying cash dividends in the foreseeable future.

The following table sets forth, for fiscal periods indicated, the range of high and low sales prices available for the years ended December 31, 2003 and 2004.

Year ended December 31, 2003	High	Low
Quarter End 3/31/03	$6.07	$2.92
Quarter End 6/30/03	$4.70	$2.75
Quarter End 9/30/03	$5.73	$3.33
Quarter End 12/31/03	$7.40	$5.48
Year ended December 31, 2004	**High**	**Low**
Quarter End 3/31/04	$7.93	$5.29
Quarter End 6/30/04	$5.40	$3.00
Quarter End 9/30/04	$3.79	$3.12
Quarter End 12/31/04	$3.77	$3.15

Item 6. *Selected Financial Data*

The following tables should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7 of this report and the financial statements and related notes included in Item 8 of this report.

(in thousands, except per share data)	Year Ended December 31, 2004	2003	2002	2001	(1) Six Months Ended December 31, 2001	Fiscal Years Ended June 30, 2001	2000	October 22, 1992 (Inception) to December 31, 2004
				(unaudited)				
Statement of Operations Data:								
Revenue	$ 2,195	$ 463	$ 57	$ 94	$ 8	$ 116	$ 58	$ 3,445
Expenses:								
Research and development	19,344	21,805	24,809	22,333	11,465	17,041	7,953	127,505
General and administrative	8,367	7,399	8,146	7,559	3,957	6,761	4,516	52,190
In-license fees	—	—	—	—	—	—	5,034	5,034
Total operating expenses	27,711	29,204	32,955	29,892	15,422	23,802	17,503	184,729
Loss from operations	(25,516)	(28,741)	(32,898)	(29,798)	(15,414)	(23,686)	(17,445)	(181,284)
Interest expense	(209)	(250)	(278)	(347)	(204)	(180)	(129)	(2,380)
Interest income	1,905	3,282	5,569	9,364	4,316	7,907	2,548	27,310
Other expense, net	(103)	(65)	(132)	(68)	(17)	(55)	(13)	(225)
Net loss	$ (23,923)	$ (25,774)	$ (27,739)	$ (20,849)	$ (11,319)	$ (16,014)	$ (15,039)	$(156,579)
Basic and diluted net loss per common share	$ (1.17)	$ (1.28)	$ (1.38)	$ (1.05)	$ (0.57)	$ (0.85)	$ (1.03)	
Shares used in basic and diluted net loss per common share calculation	20,362,155	20,149,214	20,080,998	19,845,640	19,959,941	18,730,437	14,557,999	

(in thousands)	December 31, 2004	2003	2002	2001 (1)	June 30, 2001	2000
Balance Sheet Data:						
Cash, cash equivalents, available-for-sale securities, and restricted investments	$ 76,218	$ 98,878	$ 119,224	$148,254	$157,737	$ 77,953
Working capital	63,873	86,051	107,398	137,486	151,341	72,732
Total assets	90,507	116,595	140,686	168,409	174,946	85,287
Long-term obligations	9,064	10,592	8,852	8,558	5,391	4,113
Deficit accumulated during development stage	(156,579)	(132,656)	(106,882)	(79,143)	(67,823)	(51,810)
Stockholders' equity	79,875	103,886	130,057	157,350	167,182	79,013

(1) We changed our fiscal year end from June 30 to December 31, effective December 31, 2001.

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

This Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements that involve risks and uncertainties. Avigen's actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause or contribute to such differences include, but are not limited to, those discussed herein and in "Risk Factors" under Item 1.

Overview

We are focused on developing innovative therapeutics to treat serious disorders, primarily for neurological conditions. Since our inception, we have devoted substantially all of our resources to research and development activities, primarily with early stage research in the field of gene therapy, which led to our initiation of three separate phase I clinical trials under three FDA approved INDs. We currently have one ongoing phase I/II clinical trial which uses AAV vectors to treat Parkinson's disease.

We are shifting our focus from DNA-based drugs to more conventional small molecule therapeutics and are actively seeking to identify and acquire rights to later-stage product candidates with experience in human clinical trials. Gene therapy has proven to be a challenging field. Despite our numerous discoveries and accomplishments, our development programs have uncovered new scientific challenges, and the pace of our clinical trials suggests that these programs will require more time and investment to complete. These factors have led our management to modify its near-term strategy to restructure our portfolio and focus on acquiring or licensing rights to more conventional pharmaceutical candidates.

Our History

Since our inception, our research and development activities have primarily focused on the development of our proprietary gene delivery platform technology based on adeno-associated virus vectors, known as "AAV vectors", and the development and clinical testing of our DNA-based treatments for hemophilia and certain neurological diseases. These gene delivery technologies are supported by a broad base of proprietary intellectual property that we have assembled covering methods of transferring genes into cells, high-yield processes to manufacture contaminant-free AAV vectors, specific genes of interest, specific disease indications, and other proprietary technologies and processes. In addition, we have built the manufacturing capacity necessary to produce clinical-grade AAV vectors and our other DNA-based treatments to support the research efforts and clinical trial needs of ourselves and our collaboration partners, and we believe this manufacturing capacity will also support the commercial needs of many potential gene-delivery applications.

In May 2004, we suspended subject enrollment in our phase I clinical trial for hemophilia B in order to focus our development efforts and resources on our other development programs for neurological disorders. In July 2004, in response to this strategic realignment, we reduced our staff level by 37 employees, or approximately 36%. We incurred a charge of approximately $812,000 for severance payments and other termination-related benefits and estimate that the future annual savings in personnel costs, including salaries, benefits and temporary staffing, will approximate $3.1 million.

In August 2004, we received authorization from the FDA to initiate a phase I/II clinical trial of AV201, our drug candidate for the treatment of Parkinson's disease. In December 2004, we enrolled and treated our first subject. In February 2005, after reviewing the results of our initial subject treatment with the FDA, we received clearance from the FDA to simultaneously enroll the remaining subjects in the first dose level, which we expect will result in an acceleration of the trial. Despite this recent event, we continue to expect that the regulatory review process for gene therapy programs will be uncertain, lengthy, and complex, and that the development of our gene delivery products may require longer clinical development timelines and greater investments to complete than previously anticipated.

We are a development stage company and have primarily supported the financial needs of our research and development activities since our inception through public offerings and private placements of our equity securities. We have not received any revenue from the sale of our products in development, and we do not anticipate generating revenue from the sale of products in the foreseeable future. As a result, we expect that we will need to obtain additional funding to support the anticipated future needs of our research and development activities and potential

acquisition or in-licensing of new development products. We expect our source of revenue, if any, for the next several years to consist of payments under collaborative arrangements with third parties, government grants, and license fees. We have incurred losses since our inception and expect to incur losses over the next several years due to our lack of any substantial source of revenue and the continuation of our ongoing and planned research and development efforts, including preclinical studies and clinical trials. There can be no assurance that we will successfully acquire, develop, commercialize, manufacture, or market our product candidates or ever achieve or sustain product revenues or profitability. At December 31, 2004 we had an accumulated deficit of $156.6 million and cash, cash equivalents, available-for-sale securities, and restricted investments of approximately $76.2 million. We believe that our capital resources at December 31, 2004 will be adequate to fund our current operating needs over the next three to four years.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments related to revenue recognition, valuation of investments in financial instruments, impairment of property and equipment, and allocation of research and development expenses. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described under Note 1 in the Notes to our Financial Statements, we believe the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements.

Revenue recognition

We recognize revenue associated with up-front license, technology access and research and development funding payments under collaborative agreements ratably over the relevant periods specified in the agreements, generally the development phase. This development phase can be defined as a specified period of time, however, in certain cases, the collaborative agreement specifies a development phase that culminates with milestone objectives but does not have a fixed date and requires us to estimate the time period over which to recognize this revenue. Our estimated time periods are based on management's estimate of the time required to achieve a particular development milestone considering the projected level of effort and current stage of development. If our estimate of the development-phase time period changes, the amount of revenue we recognize related to up-front payments for a given period will accelerate or decrease accordingly. For example, in March 2003, we received a $2.5 million payment from Bayer under the terms of a collaboration agreement for Coagulin-B, for hemophilia administered to the liver. The revenue associated with the payment was being recognized ratably over the development phase, which was initially estimated to be five years. In May 2004, we suspended subject enrollment in the phase I clinical trial for this product and, as a result, ended the development phase for this product and recognized as revenue $2.0 million, constituting the portion of the $2.5 million payment not previously recognized as revenue, during the quarter ended June 30, 2004.

We recognize non-refundable product license fees, including fees associated with research license agreements, for which we have no further performance obligations, and no continuing involvement requirements, on the earlier of the dates on when the payments are received or when collection is assured.

Valuation of investments in financial instruments

We carry investments in financial instruments at fair value with unrealized gains and losses included in accumulated other comprehensive income or loss in stockholders' equity. Our investment portfolio does not include equity securities or derivative financial instruments that could subject us to material market risk; however, we do

invest in corporate obligations that subject us to varying levels of credit risk. Management assesses whether declines in the fair value of investment securities are other-than-temporary. If a decline in fair value of a financial instrument is judged to be other-than-temporary, the cost basis of the individual security is written down to fair value and the amount of the write down is included in earnings. In determining whether a decline is other-than-temporary, management considers:

- the length of time and the extent to which the market value of the security has been less than cost;
- the financial condition and near-term prospects of the issuer; and
- our intention and ability to retain our investment in the issuer for a period of time sufficient to allow for any anticipated recovery in market value, which could be until maturity.

The determination of whether a decline in fair value is other-than-temporary requires significant judgment, and could have a material impact on our balance sheet and results of operations. We have not had any write-downs for other-than-temporary declines in the fair value of our financial instruments since our inception.

Impairment of property and equipment

We have invested significant amounts on construction for improvements to our research and development facilities, with the largest portion of our spending made to modify manufacturing facilities that are intended to comply with requirements of government mandated manufacturing rules for pharmaceutical production. Management assesses whether there has been any impairment in the value of these facilities. If the value of our construction for improvements is judged to be impaired, the cost basis of the property and equipment is written down to fair value and the amount of the write down is included in our net loss. In determining whether the value of our property and equipment is impaired, management considers:

- failure of manufacturing facilities and equipment to comply with government mandated policies and procedures;
- failure of the products for which the manufacturing facilities have been constructed to receive regulatory approval; and
- the extent that facilities could be idled due to the adoption of operating efficiencies for an other-than-temporary period, resulting in excess capacity.

The determination of whether the value of our property and equipment is impaired requires significant judgment, and could have a material impact on our balance sheet and results of operations. We have not had any write-downs for impairment in the value of our construction for improvements since our inception.

Research and development expenses

Our research and development expenses include certain expenses that are incurred over multiple reporting periods, such as fees for contractors and consultants, fees to collaborators for preclinical research studies, subject treatment costs related to clinical trials and related clinical manufacturing costs, and license fees for use of third-party intellectual property rights. Management assesses how much of these multi-period costs should be charged to research and development expense in each reporting period. In determining whether clinical trial activities and preclinical animal studies performed by third parties should be recognized in a specific reporting period, management considers:

- estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with the third-party service providers; and
- estimates of the percentage of work completed over the life of the individual study in accordance with discussions with internal clinical and preclinical personnel and outside service providers as to the progress or stage of completion of trials or services and the agreed upon fee to be paid for such services.

The determination of the percentage of work completed that determines the amount of research and development expense that should be recognized in a given period requires significant judgment, and could have

a material impact on our balance sheet and results of operations. These estimates may or may not match the actual services performed by the service providers as determined by subject enrollment levels, preclinical animal study schedules, and related activities. We monitor service provider activities to the extent possible; however, if we underestimated activity levels associated with various studies at a given point in time, we could record significant research and development expenses in future periods.

Results of Operations

Revenue

(In thousands, except percentages)	2004	2003	2002
Revenue	$2,195	$463	$57
Percentage increase (decrease) over prior period	374%	712%	

In 2004 and 2003, revenue primarily consisted of the recognition of $2.1 million and $375,000, respectively, of deferred revenue from the $2.5 million payment received from Bayer in 2003 in connection with our collaboration on the development of Coagulin-B for the treatment of hemophilia B to the liver. The payment was being recognized ratably over the estimated development period of the hemophilia B product candidate, which was estimated at five years from the date of the payment, or $125,000 per quarter since June 2003. In May 2004, we suspended subject enrollment in the trial, which resulted in the termination of the development period of the liver-targeted product candidate associated with the Bayer payment. We recognized the remaining $2.0 million of deferred revenue in the second quarter of 2004. Research license fees totaled $64,500, $79,000 and $38,000, respectively, during 2004, 2003, and 2002. Research license agreements allow the licensee to make or use products using our patented AAV technologies for research purposes only, and do not allow for the use of our technologies in products for commercial sale. These licenses usually include initiation fees and annual maintenance fees based on the initial date of the agreement, and therefore do not occur ratably throughout the year. Royalty revenue totaled $5,800, $9,000 and $19,000, respectively, in 2004, 2003, and 2002, all of which was attributed to a single royalty license that was entered into in July 2000, which allows for the development, manufacture, use and commercial sale of products using our patented AAV technologies.

As a result of the recognition of the remaining amount of the Bayer payment in the second quarter of 2004, and the termination of the collaboration agreement with Bayer in December 2004, we expect that our revenues for the foreseeable future will consist solely of research license fees and royalty revenue, which we expect to be immaterial.

Research and Development Expenses

Our research and development expenses can be divided into two primary functions, costs to support research and preclinical development and costs to support preparation for and implementation of human clinical trials. Research and preclinical development costs include activities associated with general research and exploration, animal studies, production of vector for use by external collaborators in general research and exploration, development of processes to translate research achievements into commercial scale capabilities, and in-house and independent third-party validation testing of potential acquisition or in-license drug candidates. Clinical development costs include activities associated with preparing for regulatory approvals, maintaining regulated and controlled processes, manufacturing vector for use in human clinical trials, and supporting subject enrollment and subject administration within clinical trials.

During the second-half of 2002, we took strategic steps to focus the work of our research and development organizations on the clinical development of our lead gene-delivery product programs. This included a reduction in staff and the implementation of other operational efficiencies without limiting our production capabilities. Our research and development staff count grew from approximately 130 at December 31, 2001 to a peak of approximately 145 in September 2002. The impact of the workforce reduction in October 2002 reduced that staff level to 90 at December 31, 2002. At December 31, 2003, our staff count dedicated to research and development activities had declined to approximately 79. In July 2004, consistent with the decision to suspend subject enrollment in the phase I clinical trial for hemophilia B, and the refocus of our resources toward our programs for serious

neurological disorders, we further reduced our total staff by approximately 36%, which reduced the number of employees dedicated to research and development activities to approximately 45 at December 31, 2004.

During 2004 and 2003, our research and preclinical development expenses included activities for our development programs for hemophilia, Parkinson's disease, neuropathic pain, and other neurological targets, as well as validation activities associated with potential acquisition or in-license of non-gene therapy drug products. During 2004 and 2003, our clinical development expenses included activities to support our gene therapy development programs for Coagulin-B for hemophilia and AV201 for Parkinson's disease. During 2002, our research and preclinical development expenses were focused on our development programs for hemophilia and Parkinson's disease, and other cardiac and neurological targets, and our clinical development expenses were focused on our development programs for Coagulin-B and AV201.

The costs associated with these two primary functions of our research and development activities approximate the following (in thousands):

	Year Ended December 31,				
	2004	2003	Percentage decrease 2004 over 2003	Year Ended December 31, 2002	Percentage decrease 2003 over 2002
Research and preclinical development	$12,612	$13,450	(6)%	$14,266	(6)%
Clinical development	6,732	8,355	(19)%	10,543	(21)%
Total research and development expenses ..	$19,344	$21,805	(11)%	$24,809	(12)%

Because a significant percentage of our research and development resources are dedicated to activities that focus on fundamental platform technologies that may be used in many different product applications, including production and administration techniques, the majority of our costs are not directly attributed to individual development programs. Decisions regarding our project management and resource allocation are primarily based on interpretations of scientific data, rather than cost allocations. Our estimates of costs between research and preclinical development and clinical development are primarily based on staffing roles within our research and development departments. As such, costs allocated to specific projects may not necessarily reflect the actual costs of those efforts and, therefore, we do not generally evaluate actual costs-incurred information on a project-by-project basis. In addition, we are unable to estimate the future costs to completion for any specific projects.

We have reclassified approximately $165,000 as clinical development expenses that were reported as research and preclinical development expenses for 2003 in our Annual Report on Form 10-K for the period ended December 31, 2003, files with the SEC on March 15, 2004. This reclassification had no impact on our results of operations.

Comparison of the Years Ended December 31, 2004 and 2003. The decrease of $838,000 in our research and preclinical development expenses for 2004, compared to 2003, was primarily due to changes in costs for the following:

- lower materials expenses of $500,000, primarily reflecting a decrease in our consumption of materials to produce AAV vectors and support our other on-going research activities as a result of the transfer of our Parkinson's program into a clinical development phase, our refocusing of our efforts on fewer gene therapy projects, and the general impact of our lower staff levels due to the staff reduction that occurred in July 2004,
- lower expenditures for services from third-party collaborators associated with our preclinical animal studies of $570,000, primarily related to the completion of a significant portion of our work with Parkinson's disease in 2003 as it transitioned into a clinical development phase in 2004,
- lower use tax of $261,000, related to payments in 2003 for materials that had not been properly assessed in previous years,
- lower recruiting and relocation expenses of $194,000, reflecting the decline in hiring and the use of relocation payment incentives in 2004 compared to 2003,

partially offset by,

- higher severance expenses of $281,000, representing $416,000 paid to employees affected by the staff reduction in July 2004, compared to $135,000 paid to an executive in 2003,
- higher facilities related expenses of $250,000, related to the rise in costs under the new building lease that went into effect in June 2003, and
- higher bonus expenses of $185,000, reflecting the accrual and payment of bonuses in 2004, compared to the reversal of accrued bonuses of $35,000 without any payment during 2003.

The decrease of $1.6 million in our clinical development expenses for 2004, compared to 2003, was primarily due to changes in costs for the following:

- lower license origination fees of $637,000, including $97,000 of non-cash charges in connection with the issuance of warrants in 2003,
- lower materials expenses of $575,000, reflecting lower levels of material consumed in 2004 for the production of clinical grade AAV vectors due to the delayed needs of our development programs at the clinical development stage,
- lower personnel-related expenses of $470,000, related to the staff reduction in July 2004 of approximately 15 employees, partially offset by higher average salaries in 2004, and
- lower facilities expenses of $255,000 due to the decrease in the allocation of space to clinical development activities in 2004,

partially offset by,

- higher expenditures for services from third-party collaborators associated with treating and monitoring subjects in our clinical trials of $225,000, primarily related to regulatory costs associated with filing for FDA approval and recruiting our first subject in our phase I clinical trial for Parkinson's disease, and
- higher severance expenses of $146,000, representing $286,000 paid to employees affected by the staff reduction in July 2004, compared to $140,000 paid to an executive in 2003.

Comparison of the Years Ended December 31, 2003 and 2002. The decrease of $816,000 in our research and preclinical development expenses for 2003, compared to 2002, was primarily due to changes in costs for the following:

- lower materials expenses of $1.1 million, primarily reflecting a decrease in our consumption of materials to produce our AAV vectors and support our on-going research activities related to our lower average staff level in 2003 when compared to the average staff level for most of 2002, as well as the benefits of operating efficiencies we have implemented over the previous two years,
- lower personnel-related expenses of $670,000, primarily reflecting the full-year impact of our lower staff levels in 2003 after the workforce reduction that occurred in October 2002, and
- lower consulting expenses of $157,000, reflecting decreased involvement by third-party service providers to support our in-house research,

partially offset by,

- higher expenditures for services from third-party collaborators associated with our preclinical animal studies of $659,000, primarily related to our work with Parkinson's disease,
- higher depreciation expenses of $253,000, reflecting the full-year impact of newly constructed facilities that were placed in service in the second half of 2002 for general and animal research, and
- higher other facilities-related expenses of $187,000, related to the rise in costs under the new building lease that went into effect in 2003 and generally higher maintenance costs.

The decrease of $2.2 million in our clinical development expenses for 2003, compared to 2002, was primarily due to changes in costs for the following:

- lower personnel-related expenses of $1.3 million, primarily reflecting the impact of our lower average staff level in 2003 after the workforce reduction in October 2002,
- lower materials expenses of $986,000 reflecting lower levels of materials consumed in 2003 for the production of clinical grade AAV vectors due to the delayed needs of our Coagulin-B clinical trial, as well as the general benefits from manufacturing efficiencies adopted over the previous two years for the production of our AAV vectors,
- lower expenditures to third-party collaborators associated with treating and monitoring subjects in our clinical trial of $509,000, reflecting the delay in treating Coagulin-B subjects in 2003, and
- lower consulting and validation services expenses of $716,000, primarily in connection with regulatory and quality assurance process improvements and validation of new cGMP facilities that were completed in 2002,

partially offset by,

- higher license origination fees of $675,000, including $97,000 of non-cash charges in connection with the issuance of warrants in 2003,
- higher depreciation expenses of $307,000, reflecting the full-year impact of newly constructed facilities that were placed in service in the second half of 2002 for cGMP manufacturing, and
- higher other facilities-related expenses of $277,000, related to the rise in costs under the new building lease that went into effect in 2003 and generally higher maintenance costs.

Total research and development expenses for 2004 were within management's expectations, taking into account the impact of the July 2004 staff reduction, the suspension of subject enrollment in the phase I clinical trial for Coagulin-B in May 2004, and the initiation of our clinical trial for Parkinson's disease, despite the delay, in December 2004. We believe delays in regulatory approvals and subject scheduling and coordination will continue to be factors that contribute to slower progress in our future clinical trials, particularly for gene-therapy related programs. If we are successful in our efforts to acquire or in-license drug candidates in later-stage development, our total research and development spending will be likely to rise in 2005 to meet the development needs of such products. However, if we are not successful in our efforts, we would expect to see total research and development spending decline in 2005 from our 2004 level in connection with the expected lower average staff levels.

General and Administrative Expenses

(In thousands, except percentages)	2004	2003	2002
General and administrative expenses	$8,367	$7,399	$8,146
Percentage increase (decrease) over prior period	13%	(9)%	

Comparison of the Years Ended December 31, 2004 and 2003. The increase of $968,000 in our general and administrative expenses in 2004, compared to 2003, was primarily due to changes in costs for the following:

- higher severance expenses of $1.0 million, approximately $900,000 of which was accrued in connection with the resignation of our former CEO in March 2004 and approximately $110,000 paid to employees affected by the staff reduction in July 2004,
- higher bonus expenses of $360,000, reflecting the accrual and payment of bonuses in 2004 compared to the reversal of $101,000 of accrued bonuses and no payments in 2003, and
- higher facilities-related expenses of $375,000 related to the rise in costs under the new building lease that went into effect in 2003,

partially offset by,

- lower personnel-related expenses of $330,000, reflecting the impact of a general decline in our average general and administrative staff level during the last year, including the resignation of our former CEO in March 2004,

- lower travel and other expenses of $200,000,
- lower recruiting expenses of $110,000, reflecting the decline in hiring in 2004, compared to 2003, and
- lower legal fees of $120,000, primarily related to patent-related litigation costs and higher corporate legal support in 2003 compared to 2004.

Comparison of the Years Ended December 31, 2003 and 2002. The decrease of $747,000 in our general and administrative expenses between 2003 and 2002 was primarily related to lower personnel-related costs of approximately $510,000 reflecting lower staff levels as a result of the October 2002 workforce reduction, lower depreciation and facilities-related expenses related to the reduction in allocation of space to our non-research and development activities of approximately $440,000 in 2003, and lower litigation-related legal fees of approximately $110,000 as a result of the settlement of our lawsuit with Research Corporation Technologies, Inc. These decreases were partially offset by higher patent-related legal fees of approximately $200,000 and higher expenses for other professional services and information services of approximately $160,000.

We expect our general and administrative expenses for 2005 to remain steady or decrease slightly from our 2004 levels, primarily due to lower average staff level. However, if we are successful in our efforts to acquire or in-license later-stage clinical development drug candidates, our expected general and administrative spending levels may increase to connection with the changing needs of the company.

Interest Income

(In thousands, except percentages)	2004	2003	2002
Interest income	$1,905	$3,282	$5,569
Percentage decrease over prior period	(42)%	(41)%	

Almost all of our interest income is generated from our investments in high-grade marketable securities of government and corporate debt. The declines in interest income between 2004 and 2003 and between 2003 and 2002 were primarily due to the decrease in our outstanding interest-bearing cash and securities balances, due to the use of such resources to fund our on-going operations, and to the decline in the average yield earned on our portfolio of investments.

Adoption of Recently Issued Accounting Standards

In March 2004, the FASB approved Emerging Issues Task Force (EITF) Issue No. 03-1, *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments."* The objective of this issue is to provide guidance for identifying other-than-temporarily impaired investments. EITF No. 03-1 also provides new disclosure requirements for investments that are deemed to be temporarily impaired. In September 2004, the FASB issued EITF No. 03-1-1, which delayed the effective date of EITF No. 03-1, with the exception of certain disclosure requirements. We do not believe that the adoption of EITF No. 03-1 will have a material impact on our financial condition and results of operations.

In December 2004, the FASB issued Statement No. 153, *"Exchanges of Nonmonetary Assets, and amendment of APB Opinion No. 29, Accounting for Nonmonetary Transactions."* FAS 153 eliminates the exception under Opinion 29 for nonmonetary exchanges of similar productive assets that do not have commercial substance, as defined by the statement. FAS 153 is effective for nonmonetary exchanges occurring in fiscal periods beginning after June 15, 2005. We do not believe the adoption of FAS 153 to have a material impact on our financial position, cash flows or results of operations.

In December 2004, the FASB issued Statement No. 123(R), ("FAS 123(R)"), *"Share-Based Payment,"* which amends FAS 123 and will be effective for public companies for interim or annual periods beginning after June 15, 2005. The new standard will require us to expense employee stock options and other share-based payments in our statements of operations. The FASB believes the use of a binomial lattice model for option valuation is capable of more fully reflecting certain characteristics of employee share options compared to the Black-Scholes options pricing model. The new standard may be adopted in one of three ways—the modified prospective transition method, a variation of the modified prospective transition method or the modified retrospective transition method. We are

currently evaluating how we will adopt the standard. We do not expect the adoption of FAS 123(R) to have a material impact on our current compensation practices or our statements of cash flows. However, we do expect that our adoption of FAS 123(R) will significantly increase our reported operating expenses which would have a material impact on our results of operations and related financial position for all periods after adoption.

Deferred Income Tax Assets

In accordance with FAS 109, "*Accounting for Income Taxes*," which is described in the Notes to our Financial Statements, we have calculated a deferred tax asset based on the potential future tax benefit we may be able to realize in future periods as a result of the significant tax losses experienced since our inception. However, the value of such deferred tax asset must be calculated using the tax rates expected to apply to the taxable income in the years in which such income occurs. Since we have no history of earnings, and cannot reliably predict when we might create taxable income, if at all, we have recorded a valuation allowance for the full amount of our calculated deferred tax asset.

Liquidity and Capital Resources

Since our inception in 1992, cash expenditures have significantly exceeded our revenue. We have funded our operations primarily through public offerings and private placements of our equity securities. After our initial public offering in May 1996, we raised $189 million from private placements and public offerings of our common stock and warrants to purchase our common stock, and from the receipt of $2.5 million in research support from Bayer Corporation in March 2003. After our initial public offering, we also received additional monies as a result of exercises of previously issued warrants and options to purchase our common stock, including an additional $2.1 million during the three-year-period ended December 31, 2004. The timing of and amounts realized from the exercise of these warrants and options are determined by the decisions of the respective warrant and option holders, and are not controlled by us. Therefore, funds received from exercises of stock options and warrants in past periods should not be considered an indication of additional funds to be received in the future periods. In addition, a significant percentage of options and warrants currently outstanding have exercise prices that exceed the current trading price of our common stock, and so unless the trading price of our common stock increases significantly, those options and warrants may never be exercised.

In addition to funding our operations through sales of our common stock, we have attempted to contain costs and reduce cash flow requirements by renting scientific equipment and facilities, contracting with third parties to conduct research and development and using consultants, where appropriate. We expect to incur additional future expenses, resulting in significant additional cash expenditures, as we continue our research and development activities, including our efforts to acquire or in-license later-stage clinical development drug candidates, and undertake additional preclinical studies and clinical trials of our product candidates. We also expect to incur substantial additional expenses relating to the filing, prosecution, maintenance, defense and enforcement of patent and other intellectual property claims.

At December 31, 2004, we had cash, cash equivalents, available-for-sale securities, and restricted investments, of approximately $76.2 million, compared to approximately $98.9 million at December 31, 2003 and $119.2 million at December 31, 2002. At December 31, 2004, 2003 and 2002, $11.9 million, $11.9 million, and $11.5 million, respectively, was pledged to secure certain long-term liabilities. At December 31, 2004, 2003, and 2002, these long-term liabilities included $10.0 million for our line of credit, and $1.5 million for equipment operating leases. At December 31, 2004 and 2003, these long-term liabilities also included approximately $428,000 for letters of credit which serve as security deposits on our building lease. Our restricted investments are reported as a long-term asset and would not be considered a current source of additional liquidity.

For the years ended December 31, 2004, 2003, and 2002, respectively, net cash used in operating activities was $21.8 million, $19.3 million, and $24.2 million. The decrease is primarily due to the reduction in our net loss from $27.7 million in 2002 to $25.8 million in 2003 and $23.9 million in 2004. The cash used in operating activities was primarily used to support our internal research and development activities, as well as preclinical studies and clinical trials performed by third parties. The level of cash used for operating activities during 2004 was slightly lower than management's expectations at the beginning of the year due to the general delays in the progress of our clinical trials. In 2003, net cash used in operating activities included the receipt of a $2.5 million payment from Bayer Corporation in March 2003, which was recorded as deferred revenue.

For the year ended December 31, 2004, $22.1 million and $512,000 was provided by investing and financing activities, respectively. The cash provided by investing activities consisted primarily of sales and maturities, net of purchases, of available-for-sale securities, offset to a small degree by purchases of property and equipment of $467,000. The cash provided by financing activities consisted of proceeds from the exercise of stock options and warrants during the period.

For the year ended December 31, 2003, $13.1 million and $718,000 was provided by investing and financing activities, respectively. The cash provided by investing activities consisted primarily of sales and maturities, net of purchases, of available-for-sale securities, offset to a small degree by purchases of property and equipment of $555,000 and increases in restricted investments of $428,000. The cash provided by financing activities consisted of proceeds from the exercise of stock options and warrants during the period.

For the year ended December 31, 2002, $18.0 million and $860,000 was provided by investing and financing activities, respectively. The cash provided by investing activities consisted primarily of sales and maturities, net of purchases, of available-for-sale securities, offset to a degree by purchases of property and equipment of $5.0 million and increases in restricted investments of $1.5 million. The cash provided by financing activities consisted of proceeds from the exercise of stock options and warrants during the period.

In July 2004, we eliminated 37 staff positions, thereby reducing our staff level to approximately 66 employees in order to reduce our ongoing operating expenses and extend the life of our current financial resources. The eliminated positions were primarily in research and development areas and resulted in approximately $812,000 in severance payments and other termination-related benefits, of which approximately $110,000 was included in general and administrative expenses and $702,000 was included in research and development expenses. All severance-related costs were paid in 2004. We believe that the future annual savings in personnel costs, including salaries, benefits, and temporary staffing, related to the impact of this staff reduction will approximate $3.1 million.

The following are contractual commitments at December 31, 2004 associated with debt obligations, lease obligations, and contractual commitments to fund third-party research (in thousands):

	Payments Due by Period				
Contractual Commitment	Total	Less than 1 year	1-3 years	3-5 years	After 5 years
Revolving line of credit	$ 8,000	$ —	$ 8,000	$ —	$ —
Operating leases	12,552	2,691	5,103	3,496	1,262
Research funding for third-parties	646	646	—	—	—
Total	$21,198	$3,337	$13,103	$3,496	$1,262

In June 2004, we amended the terms of our $10.0 million revolving line of credit which had been put in place with Wells Fargo Bank in June 2000, to provide support for construction-related activities, and subsequently amended in June 2002. Under the terms of the current amendment, the expiration date of the borrowing was extended from June 1, 2005 to June 1, 2007, thereby deferring the timetable to repay principal borrowed for two years. The debt instrument bears interest at a floating rate based on the London Inter-Bank Offered Rate, which is reset in three-month increments after the date of each drawdown, until such expiration. As of December 31, 2004 and 2003, the average annual rate of interest charged on the borrowing was approximately 2.70% and 2.75%, respectively. Also under the terms of this agreement, we pledged a portion of our portfolio of available for sale securities as collateral and have identified the amount of the pledged securities as restricted investments on our balance sheets. The amount of the pledged securities is equal to the amount of utilized borrowing capacity on the line of credit. At December 31, 2004, we had borrowed $8 million from the line of credit and had reserved the remaining $2.0 million in borrowing capacity to secure a letter of credit in connection with the property lease entered into in November 2000. As a result, at December 31, 2004, we have no more borrowing capacity under this facility.

Our current office and facility includes approximately 112,500 square feet of space. Of this, approximately 45,000 square feet of space is leased through May 2008 and approximately 67,500 square feet of space is leased through November 2010. Payments scheduled under these lease commitments are included in the table above under operating leases.

We enter into commitments to fund collaborative research and clinical work performed by third parties. While these contracts are cancelable by either party, we expect the research studies and clinical work to be completed

as defined in the terms of the agreements, and all amounts paid when due. Payments scheduled to be made under these contracts are included in the table above under research funding for third-parties.

We have announced that we are actively seeking to broaden our portfolio of drug development candidates through an acquisition or in-licensing program, and that this effort has identified several validated compounds that are being investigated, some of which have experience in human clinical trials. If we are successful in in-licensing or otherwise acquiring compounds, and we pay for such programs in cash, our capital resources will be reduced. Further, any in-license of compounds in greater amounts than we currently project could cause our expenses to increase beyond our current expectations.

We believe we will continue to require substantial additional funding in order to complete the research and development activities currently contemplated and to commercialize our proposed products. We believe that with the implementation of the staff reduction in July 2004 and our projected lower levels of spending to support on-going operations, our capital resources at December 31, 2004 will be adequate to fund our current operating needs for approximately three to four years. However, this forward-looking statement is based upon our current plans and assumptions regarding our future operating and capital requirements, which may change. Our future operating and capital requirements will depend on many factors, including:

- how successful, if at all, we are at acquiring or in-licensing compounds, and the nature of the consideration we pay for in-licensing compounds;
- continued scientific progress in research and development programs;
- the scope and results of preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing, prosecuting and enforcing patents claims and other intellectual property rights;
- competing technological developments;
- the cost of manufacturing scale-up;
- the costs of commercialization activities; and
- other factors which may not be within our control.

We intend to continue to seek additional funding through public or private equity or debt financing, when market conditions allow, or through additional collaborative arrangements with corporate partners. If we raise additional funds by issuing equity securities, there may be further dilution to existing stockholders. We cannot assure our investors that we will be able to enter into such financing arrangements on acceptable terms or at all. Without such additional funding, we may be required to delay, reduce the scope of, or eliminate one or more of our research or development programs.

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

Our exposure to market rate risk for changes in interest rates relates primarily to our investment portfolio and our long-term debt. We do not hold derivative financial investments, derivative commodity investments or other financial investments or engage in foreign currency hedging or other transactions that expose us to other market risks. None of our investments are held for trading purposes. Our investment objectives are focused on preservation of principal and liquidity. By policy, we manage our exposure to market risks by limiting investments to high quality issuers and highly liquid instruments with effective maturities of less than three years, and an average aggregate portfolio duration of approximately one year. Our entire portfolio is classified as available-for-sale and, as of December 31, 2004, consisted of approximately 95% fixed-rate securities and 5% variable-rate securities. This compares to approximately 93% fixed-rate securities and 7% variable-rate securities at December 31, 2003.

We have evaluated the risk associated with our portfolios of investments in marketable securities and have deemed this market risk to be immaterial. If market interest rates were to increase by 100 basis points, or 1%, from their December 31, 2004 levels, we estimate that the fair value of our securities portfolio would decline by

approximately $740,000. Our estimated exposure at December 31, 2004 is lower than our estimated $1.1 million exposure at December 31, 2003 due to the reduction in size of our overall portfolio. The modeling technique used measures duration risk sensitivity to estimate the potential change in fair value arising from an immediate hypothetical shift in market rates and quantifies the ending fair market value including principal and accrued interest.

Our long-term debt includes a $10.0 million revolving line of credit due June 1, 2007, of which we have drawn down $8.0 million in cash that will need to be repaid. Interest charged on the borrowing is based on LIBOR and is reset in three-month increments based on the date of each original drawdown. As of December 31, 2004, the average annual rate of interest charged on the borrowing was approximately 2.70% compared to 2.75% as of December 31, 2003.

Item 8. ***Financial Statements and Supplementary Data***

INDEX TO FINANCIAL STATEMENTS

The following financial statements are filed as part of this Report on Form 10-K. Condensed supplementary data for each of the quarters in the years ended December 31, 2004 and 2003 are set forth under Note 12 of our financial statements.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Avigen, Inc.

We have audited the accompanying balance sheets of Avigen, Inc. (a development stage company) as of December 31, 2004 and 2003, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2004 and for the period from inception (October 22, 1992) through December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Avigen, 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 and for the period from inception (October 22, 1992) through December 31, 2004, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Avigen Inc.'s 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 and our report dated March 10, 2005 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
March 10, 2005

AVIGEN, INC.
(a development stage company)

BALANCE SHEETS
(in thousands, except share and per share information)

	December 31, 2004	December 31, 2003
ASSETS		
Current assets:		
Cash and cash equivalents	$ 3,217	$ 2,384
Available-for-sale securities	61,073	84,566
Accrued interest	708	774
Prepaid expenses and other current assets	443	444
Total current assets	65,441	88,168
Restricted investments	11,928	11,928
Property and equipment, net	12,497	15,641
Deposits and other assets	641	858
Total assets	$ 90,507	$ 116,595
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and other accrued liabilities	$ 641	$ 1,140
Accrued compensation and related expenses	927	477
Deferred revenue — current	—	500
Total current liabilities	1,568	2,117
Long-term loan payable	8,000	8,000
Deferred rent	1,064	967
Deferred revenue	—	1,625
Commitments		
Stockholders' equity		
Preferred stock, $0.001 par value, 5,000,000 shares authorized, none issued and outstanding, in 2004 and 2003	—	—
Common stock, $0.001 par value, 50,000,000 shares authorized, and 20,381,250 and 20,276,394 shares issued and outstanding at December 31, 2004 and 2003, respectively	20	20
Additional paid-in capital	236,959	236,120
Accumulated other comprehensive (loss) income	(525)	402
Deficit accumulated during development stage	(156,579)	(132,656)
Total stockholders' equity	79,875	103,886
Total liabilities and stockholders' equity	$ 90,507	$ 116,595

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF OPERATIONS
(in thousands, except for share and per share information)

	Year Ended December 31,			Period from October 22, 1992 (inception) through December 31, 2004
	2004	2003	2002	
Revenue	$ 2,195	$ 463	$ 57	$ 3,445
Operating expenses:				
Research and development	19,344	21,805	24,809	127,505
General and administrative	8,367	7,399	8,146	52,190
In-license fees	—	—	—	5,034
Total operating expenses	27,711	29,204	32,955	184,729
Loss from operations	(25,516)	(28,741)	(32,898)	(181,284)
Interest expense	(209)	(250)	(278)	(2,380)
Interest income	1,905	3,282	5,569	27,310
Other expense, net	(103)	(65)	(132)	(225)
Net loss	$ (23,923)	$ (25,774)	$ (27,739)	$(156,579)
Basic and diluted net loss per common share	$ (1.17)	$ (1.28)	$ (1.38)	
Shares used in basic and diluted net loss	20,362,155	20,149,214	20,080,998	

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY

Period from October 22, 1992 (inception) through December 31, 2004
(in thousands, except for share information)

	Preferred Stock		Common Stock		Class B Convertible Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at October 22, 1992 (inception)	—	$—	—	$—	—	$—	$ —	$—	$ —	$ —
Issuance of common stock at $.004 per share in November and December 1992	—	—	896,062	1	—	—	4	—	—	5
Issuance of common stock at $.554 per share from January to June 1993 for services rendered	—	—	20,316	—	—	—	11	—	—	11
Issuance of common stock at $.004 to $.222 per share from November 1992 to March 1993 for cash	—	—	1,003,406	1	—	—	54	—	—	55
Issuance of Class B common stock at $.004 per share in December 1992 for cash	—	—	—	—	90,293	—	1	—	—	1
Issuance of Series A preferred stock at $4.43 per share from March to June 1993 for cash (net of issuance costs of $410,900)	678,865	1	—	—	—	—	2,595	—	—	2,596
Issuance of Series A preferred stock at $3.85 per share in March 1993 for cancellation of note payable and accrued interest	68,991	—	—	—	—	—	266	—	—	266
Issuance of common stock at $.004 per share in November 1993 pursuant to antidilution rights	—	—	22,869	—	—	—	1	—	—	1
Issuance of Series A preferred stock at $4.43 per share from July to November 1993 for cash and receivable (net of issuance costs of $187,205)	418,284	—	—	—	—	—	1,665	—	—	1,665
Issuance of Series B preferred stock at $5.54 per share in March 1994 for cash (net of issuance costs of $34,968)	128,031	—	—	—	—	—	674	—	—	674
Issuance of Series C preferred stock at $4.87 per share from July 1994 to June 1995 for cash and receivables (net of issuance costs of $259,620)	739,655	1	—	—	—	—	3,344	—	—	3,345
Issuance of Series C preferred stock at $4.87 per share in June 1995 for cancellation of notes payable	35,500	—	—	—	—	—	173	—	—	173
Net loss and comprehensive loss from inception to June 30, 1995	—	—	—	—	—	—	—	—	(8,608)	(8,608)
Balance at June 30, 1995 (carried forward)	2,069,326	2	1,942,653	2	90,293	—	8,788	—	(8,608)	184

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY (Continued)

Period from October 22, 1992 (inception) through December 31, 2004
(in thousands, except for share information)

	Preferred Stock		Common Stock		Class B Convertible Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at June 30, 1995 (brought forward)	2,069,326	2	1,942,653	2	90,293	—	8,788	—	(8,608)	184
Issuance of Series C preferred stock at $4.87 per share in July 1995 for cash (net of issuance costs of $26,000)	41,042	$—	—	$—	—	$—	$ 174	$—	$ —	$ 174
Issuance of Series D preferred stock at $7.09 per share from October 1995 to February 1996 for cash (net of issuance costs of $25,279)	205,351	—	—	—	—	—	1,430	—	—	1,430
Issuance of Series D preferred stock at $7.09 per share in March 1996 in settlement of accounts payable	22,574	—	—	—	—	—	160	—	—	160
Issuance of common stock at $.004 per share in March 1996 pursuant to antidilution rights	—	—	17,630	—	—	—	1	—	—	1
Issuance of stock options in February 1996 in settlement of certain accrued liabilities	—	—	—	—	—	—	137	—	—	137
Conversion of Class B common stock to common stock	—	—	231,304	1	(90,293)	—	(1)	—	—	—
Issuance of warrants to purchase common stock in connection with 1996 bridge financing in March 1996	—	—	—	—	—	—	300	—	—	300
Conversion of preferred stock to common stock in May 1996	(2,338,293)	(2)	2,355,753	2	—	—	(1)	—	—	(1)
Issuance of common stock at $8.00 per share in connection with the May 1996 initial public offering (net of issuance costs of $798,414 and underwriting discount of $1,500,000)	—	—	2,500,000	2	—	—	17,699	—	—	17,701
Proceeds from exercise of options at $0.44 per share in June 1996	—	—	6,178	—	—	—	3	—	—	3
Repurchase of common stock	—	—	(18,325)	—	—	—	(1)	—	—	(1)
Deferred compensation	—	—	—	—	—	—	164	—	—	164
Amortization of deferred compensation	—	—	—	—	—	—	(128)	—	—	(128)
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	(4,097)	(4,097)
Balance at June 30, 1996 (carried forward)	—	—	7,035,193	7	—	—	28,725	—	(12,705)	16,027

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY (Continued)

Period from October 22, 1992 (inception) through December 31, 2004
(in thousands, except for share information)

	Preferred Stock		Common Stock		Class B Convertible Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at June 30, 1996 (brought forward)	—	—	7,035,193	7	—	—	28,725	—	(12,705)	16,027
Issuance of common stock at $8.00 per share in July 1996 in connection with the exercise of underwriters' over- allotment option (net of underwriting discount of $150,000)	—	$ —	250,000	$—	—	$—	$ 1,850	$—	$ —	$ 1,850
Proceeds from exercise of options at $0.44 to $0.71 per share	—	—	3,387	—	—	—	1	—	—	1
Amortization of deferred compensation	—	—	—	—	—	—	41	—	—	41
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	(5,578)	(5,578)
Balance at June 30, 1997	—	—	7,288,580	7	—	—	30,617	—	(18,283)	12,341
Proceeds from exercise of options at $0.44 to $0.71 per share	—	—	17,278	—	—	—	10	—	—	10
Amortization of deferred compensation	—	—	—	—	—	—	41	—	—	41
Compensation expense related to options granted for services	—	—	—	—	—	—	68	—	—	68
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	(8,877)	(8,877)
Balance at June 30, 1998	—	—	7,305,858	7	—	—	30,736	—	(27,160)	3,583
Proceeds from exercise of options at $0.44 to $4.31 per share	—	—	181,045	—	—	—	222	—	—	222
Amortization of deferred compensation	—	—	—	—	—	—	41	—	—	41
Issuance of common stock at $2.25–$2.94 per share and warrants in August to September 1998 in connection with a Private Placement (net of issuance cost of $233,584)	—	—	1,306,505	1	—	—	2,734	—	—	2,735
Issuance of common stock at $3.81–$4.88 per share and warrants in December 1998 in connection with a Private Placement (net of issuance cost of $438,183)	—	—	1,367,280	2	—	—	5,195	—	—	5,197
Issuance of common stock at $5.50–$6.00 per share and warrants in February to April 1999 in connection with a Private Placement (net of issuance cost of $1,033,225)	—	—	2,198,210	2	—	—	12,154	—	—	12,156
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	(9,611)	(9,611)
Balance at June 30, 1999 (carried forward)	—	—	12,358,898	12	—	—	51,082	—	(36,771)	14,323

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY (Continued)

Period from October 22, 1992 (inception) through December 31, 2004
(in thousands, except for share information)

	Preferred Stock		Common Stock		Class B Convertible Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at June 30, 1999 (brought forward)	—	—	12,358,898	12	—	—	51,082	—	(36,771)	14,323
Proceeds from exercise of options at $0.44 to $15.50	—	$ —	440,259	$ 1	—	$—	$ 1,533	$ —	$ —	$ 1,534
Proceeds from exercise of warrants at $2.81 to $31.95	—	—	1,017,215	1	—	—	8,427	—	—	8,428
Amortization of deferred compensation	—	—	—	—	—	—	5	—	—	5
Compensation expense related to options granted for services	—	—	—	—	—	—	89	—	—	89
Warrants granted for patent licenses	—	—	—	—	—	—	3,182	—	—	3,182
Warrants granted for building lease	—	—	—	—	—	—	1,738	—	—	1,738
Issuance of common stock at $16.19 to $25.56 per share and warrants in October and November 1999 in connection with a Private Placement (net of issuance cost of $2,804,255)	—	—	2,033,895	2	—	—	37,220	—	—	37,222
Issuance of common stock at $26 per share in April and May 2000 in connection with a Public Offering (net of issuance cost of $2,288,966)	—	—	1,150,000	1	—	—	27,610	—	—	27,611
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	(15,039)	(15,039)
Net unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(80)	—	(80)
Comprehensive loss	—	—	—	—	—	—	—	—	—	(15,119)
Balance at June 30, 2000 (carried forward)	—	—	17,000,267	17	—	—	130,886	(80)	(51,810)	79,013

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY (Continued)

Period from October 22, 1992 (inception) through December 31, 2004
(in thousands, except for share information)

	Preferred Stock		Common Stock		Class B Convertible Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at June 30, 2000 (brought forward)	—	—	17,000,267	17	—	—	130,886	(80)	(51,810)	79,013
Proceeds from exercise of options at $0.44 to $34.00 per share	—	$—	165,700	$—	—	$—	$ 869	$ —	$ —	$ 869
Proceeds from exercise of warrants at $2.18 to $23.43	—	—	174,255	1	—	—	771	—	—	772
Compensation expense related to options granted for services	—	—	—	—	—	—	336	—	—	336
Issuance of common stock at $37.50 to $45.06 per share in November 2000 Public Offering (net of issuance cost of $4,622,188)	—	—	2,291,239	2	—	—	86,084	—	—	86,086
Issuance of common stock at $47.82 per share in February 2001 pursuant to a collaboration agreement	—	—	313,636	—	—	—	15,000	—	—	15,000
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	(16,014)	(16,014)
Net unrealized gain on available-for-sale securities	—	—	—	—	—	—	—	1,120	—	1,120
Comprehensive loss	—	—	—	—	—	—	—	—	—	(14,894)
Balance at June 30, 2001	—	—	19,945,097	20	—	—	233,946	1,040	(67,824)	167,182
Proceeds from exercise of options at $2.13 to $6.75 per share	—	—	11,282	—	—	—	60	—	—	60
Proceeds from exercise of warrants $7.50 per share	—	—	9,955	—	—	—	75	—	—	75
Compensation expense related to options granted for services	—	—	—	—	—	—	179	—	—	179
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	(11,319)	(11,319)
Net unrealized gain on available-for-sale securities	—	—	—	—	—	—	—	1,173	—	1,173
Comprehensive loss	—	—	—	—	—	—	—	—	—	(10,146)
Balance at December 31, 2001	—	—	19,966,334	20	—	—	234,260	2,213	(79,143)	157,350
Proceeds from exercise of options at $1.875 to $8.525 per share	—	—	34,627	—	—	—	113	—	—	113
Proceeds from exercise of warrants at $7.50 per share	—	—	99,585	—	—	—	747	—	—	747
Compensation expense related to options granted for services	—	—	—	—	—	—	217	—	—	217
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	(27,739)	(27,739)
Net unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(631)	—	(631)
Comprehensive loss	—	—	—	—	—	—	—	—	—	(28,370)
Balance at December 31, 2002 (carried forward)	—	—	20,100,546	20	—	—	235,337	1,582	(106,882)	130,057

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY (Continued)

Period from October 22, 1992 (inception) through December 31, 2004
(in thousands, except for share information)

	Preferred Stock		Common Stock		Class B Convertible Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2002 (brought forward)	—	—	20,100,546	20	—	—	235,337	1,582	(106,882)	130,057
Proceeds from exercise of options at $2.12 to $6.50 per share	—	—	63,746	—	—	—	242	—	—	242
Proceeds from exercise of warrants at $2.47 to $6.09 per share	—	—	112,102	—	—	—	476	—	—	476
Compensation expense related to options granted for services	—	—	—	—	—	—	65	—	—	65
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	(25,774)	(25,774)
Net unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(1,180)	—	(1,180)
Comprehensive loss										(26,954)
Balance at December 31, 2003	—	—	20,276,394	$20	—	—	236,120	402	(132,656)	103,886
Proceeds from exercise of options at $0.443 to $6.313 per share	—	—	86,856	—	—	—	403	—	—	403
Proceeds from exercise of warrants at $6.05 per share	—	—	18,000	—	—	—	109	—	—	109
Compensation expense related to options granted for services	—	—	—	—	—	—	230	—	—	230
Warrants granted for patent licenses	—	—	—	—	—	—	97	—	—	97
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	(23,923)	(23,923)
Net unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(927)	—	(927)
Comprehensive loss										(24,850)
Balance at December 31, 2004	—	$—	20,381,250	$20	—	$—	$236,959	$ (525)	$(156,579)	$ 79,875

See accompanying notes.

AVIGEN, INC.
(a development stage company)

STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,			Period from October 22, 1992 (inception) through December 31,
	2004	2003	2002	2004
Operating Activities				
Net loss	$(23,923)	$(25,774)	$(27,739)	$(156,579)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	3,610	3,640	3,136	15,977
Amortization of deferred compensation	—	—	—	164
Non-cash rent expense for warrants issued in connection with the extension of the building lease	217	217	217	1,049
Amortization of deferred rent	97	115	294	951
Non-cash compensation expense for common stock, warrants, and stock options issued for services	230	65	217	1,705
Warrants issued for patent license	—	—	—	3,182
Changes in operating assets and liabilities:				
Accrued interest	66	219	342	(524)
Prepaid expenses and other current assets	1	14	(60)	(627)
Deposits and other assets	—	210	107	(26)
Accounts payable, other accrued liabilities and accrued compensation and related expenses	49	(160)	(724)	2,078
Deferred revenue	(2,125)	2,125	—	—
Net cash used in operating activities	$(21,778)	$(19,329)	$(24,210)	$(132,650)
Investing Activities				
Purchases of property and equipment	(467)	(555)	(5,049)	(28,178)
Increase in restricted investments	—	(428)	(1,500)	(11,928)
Purchases of available-for-sale securities	(79,670)	(84,129)	(82,242)	(705,085)
Maturities of available-for-sale securities	102,236	98,228	106,809	643,489
Net cash provided by (used in) investing activities	22,099	13,116	18,018	(101,702)
Financing Activities				
Proceeds from long-term obligations	—	—	—	10,133
Repayment of long-term obligations	—	—	—	(1,710)
Proceeds from bridge financing	—	—	—	1,937
Repayment of bridge financing	—	—	—	(2,131)
Payments on capital lease obligations	—	—	—	(2,154)
Proceeds from sale-leaseback of equipment	—	—	—	1,927
Proceeds from issuance preferred stock, net of issuance costs	—	—	—	9,885
Proceeds from warrants and options exercised	512	718	860	14,063
Proceeds from issuance of common stock, net of issuance costs and repurchases	—	—	—	205,619
Net cash provided by financing activities	512	718	860	237,569
Net increase (decrease) in cash and cash equivalent	833	(5,495)	(5,332)	3,217
Cash and cash equivalents, beginning of period	2,384	7,879	13,211	—
Cash and cash equivalents, end of period	$ 3,217	$ 2,384	$ 7,879	$ 3,217
Supplemental disclosure				
Issuance of preferred stock for cancellation of accounts payable, notes payable and accrued interest	$ —	$ —	$ —	$ 499
Issuance of stock options for repayment of certain accrued liabilities	$ —	$ —	$ —	$ 137
Issuance of warrants in connection with bridge financing	$ —	$ —	$ —	$ 300
Issuance of warrants in connection with the extension of the building lease	$ —	$ —	$ —	$ 1,738
Deferred compensation related to stock option grants	$ —	$ —	$ —	$ 164
Purchase of property and equipment under capital lease financing	$ —	$ —	$ —	$ 226
Cash paid for interest	$ 209	$ 250	$ 278	$ 1,887

See accompanying notes.

NOTES TO FINANCIAL STATEMENTS

1. Summary of Significant Accounting Policies

Description of Business and Basis of Presentation

Avigen, Inc. was incorporated on October 22, 1992 in Delaware and is focused on developing innovative therapeutics to treat serious disorders, primarily for neurological conditions. We have developed proprietary DNA-based drug delivery technologies, including our proprietary gene-delivery platform based on adeno-associated virus (AAV) vectors. We are actively pursuing the acquisition or in-licensing of later-stage drug development candidates of more conventional pharmaceutical drugs that compliment our focus on neurological diseases.

We are also currently using our DNA-based drug delivery technologies to develop a novel gene therapeutic for advanced Parkinson's disease and are enrolling subjects in a phase I/II clinical trial. Since our inception, our activities have consisted principally of acquiring product rights, raising capital, establishing facilities and performing research and development. Accordingly, we are considered to be in the development stage. We operate in a single segment.

At December 31, 2004, we had an accumulated deficit of $156.6 million and expect to continue to incur substantial losses over the next several years while we continue in this development stage. We plan to meet our capital requirements primarily through issuances of equity securities, payments under collaborative agreements with third parties, government grants, and license fees. We intend to seek additional funding through public or private equity or debt financing, when market conditions allow. There can be no assurance that we will be able to enter into financing arrangements on acceptable terms in the future, if at all.

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires our management to make judgments, assumptions and estimates that affect the amounts reported in our financial statements and the accompanying notes. Actual results could differ materially from those estimates.

Cash and Cash Equivalents

We consider all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. These amounts are recorded at cost, which approximates fair market value.

Available- for-Sale Securities

We invest our excess cash balances in marketable securities, primarily corporate debt securities, federal agency obligations, asset-backed securities, U.S. treasuries, and municipal bonds, with the primary investment objectives of preservation of principal, a high degree of liquidity, and maximum total return. We have classified our investments in marketable securities as available-for-sale. Available-for-sale securities are reported at market value and unrealized holding gains and losses, net of the related tax effect, if any, are excluded from earnings and are reported in other comprehensive income and as a separate component of stockholders' equity until realized. A decline in the market value of a security below its cost that is deemed to be other than temporary is charged to earnings, and would result in the establishment of a new cost basis for the security.

Our available-for-sale securities consist principally of obligations with a minimum short-term rating of A1/P1 and a minimum long-term rating of A- and with effective maturities of less than three years. The cost of securities sold is based on the specific identification method. Interest on securities classified as available for sale is included in interest income.

Fair value of financial instruments

The fair value of our cash equivalents and available-for-sale securities is based on quoted market prices. The fair value of our loans payable is based on current interest rates available to us for debt instruments with similar terms, degrees of risk, and remaining maturities. The carrying amount of our cash equivalents, available-for-sale securities and loan payable are considered to be representative of their respective fair value at December 31, 2004 and 2003.

Restricted Investments

In June 2000, we initially entered into a financing arrangement to support construction related activities. Under this arrangement, we have pledged $10.0 million of our portfolio of available-for-sale securities to secure this long-term obligation.

In January 2002, we also entered into equipment operating leases for certain research and development equipment. Under the terms of these leases, we have pledged $1.5 million of our portfolio of available-for-sale securities to secure these equipment operating leases.

In May 2003, we secured two letters of credit to serve as security deposits in connection with a building lease that became effective July 1, 2003. This building lease was executed in February 2000 and replaced our previous building lease and sublease on the same premises that expired June 30, 2003 under the original terms of the agreements. Under the terms of these letters of credit, we have pledged $428,000 of our portfolio of available-for-sale securities to secure these letters of credit.

At December 31, 2004 and 2003, $11.9 million was classified as restricted investments in long term assets, representing the combined aggregate portion of our portfolio of available-for-sale securities that were pledged in connection with these long-term liabilities.

Concentration of Credit Risk

Cash, cash equivalents, available-for-sale securities and restricted investments consist of financial instruments that potentially subject us to concentrations of credit risk to the extent of the value of the assets recorded on the balance sheet. We believe that we have established guidelines for investment of our excess cash that maintain safety and liquidity through our policies on diversification among asset classes and issuers, as well as across investment maturities.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation and amortization are provided using the straight-line method over the estimated useful lives of the respective assets, or in the case of leasehold improvements, over the lesser of the estimated useful lives or the remaining lease terms. The estimated useful lives of our property and equipment range from three to seven years.

Expenses for repairs and maintenance are charged to operations as incurred. Upon retirement, disposition, or sale, the cost of the property and equipment disposed of and the related accumulated depreciation are deducted from the accounts, and any resulting gain or loss is credited or charged to operations.

Revenue Recognition

We record revenue associated with up-front license, technology access, and research and development funding payments under collaboration agreements for the development of our product candidates ratably over the relevant periods specified in the agreements, generally the development phase. The development phase can be defined as a specified period of time, however, in certain cases, the collaborative agreement specifies a development phase that culminates with milestone objectives but does not have a fixed date, which requires us to estimate the

development period of those product candidates. The estimate of the development period may be revised as additional information is received or actual results differ from expectations. For example, in March 2003, we received a $2.5 million payment from Bayer Corporation under the terms of our collaboration agreement for the development of Coagulin-B, our product candidate that we were developing for the treatment of hemophilia B, involving administration to the liver. This amount was recorded as deferred revenue and was being recognized as revenue ratably over the estimated development period for this product, which was determined to be five years, or approximately $125,000 per quarter.

In May 2004, we announced the suspension of subject enrollment in our phase I clinical trial involving the administration of Coagulin-B to the liver. This resulted in the termination of the development of the liver-targeted product candidate associated with the March 2003 Bayer payment. As a result, we accelerated the recognition of the remaining $2.0 million of deferred revenue in our statements of operations for the year ended December 31, 2004.

We record grant revenue in the period in which the revenue is earned as defined by the grant agreement. Since our inception, we have recognized approximately $690,000 of grant revenue, which includes amounts earned pursuant to reimbursements under government grants, of which all have come from the National Institutes of Health.

We record royalty revenue from license agreements as earned in accordance with the contract terms when third-party results can be reliably determined and collectibility is reasonably assured. We have recorded approximately $35,000 in royalty revenue in connection with sales from a third party of products that utilize our AAV technologies over the last four years. These products are sold for research purposes only and were primarily sold within the U.S.

Non-refundable product license fees, including fees associated with research license agreements, for which we have no further performance obligations, and no continuing involvement requirements, are recognized on the earlier of when the payments are received or when collection is assured. We have recorded approximately $220,000 in research license fees since our inception.

Comprehensive Loss

Components of other comprehensive loss, including unrealized gains and losses on available-for-sale investments, were included as part of total comprehensive loss. For all periods presented, we have disclosed comprehensive loss in the statement of stockholders' equity.

Research and Development Expenses

Research and development costs are charged to expense in the period incurred and include related salaries and benefits, laboratory materials, clinical trial and related clinical-trial-manufacturing costs, contract and outside service fees, and facilities and overhead costs. Research and development expenses consist of costs incurred for our independent, as well as our collaborative, research and development activities.

Clinical development costs are a significant component of research and development expenses. We accrue costs for clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with the clinical trial sites. We determine our estimates through discussion with internal clinical personnel and outside service providers as to the progress or stage of completion of trials or services and the agreed upon fee to be paid for such services. These estimates may or may not match the actual services performed by the organizations as determined by subject enrollment levels and related activities. We monitor clinical trial activities to the extent possible; however, if we underestimated activity levels associated with various studies at a given point in time, we could record significant research and development expenses in future periods.

Income Taxes

Income taxes are accounted for in accordance with FAS 109, *Accounting for Income* Taxes, which requires the use of the liability method. Deferred tax assets and liabilities are provided for temporary differences between the financial reporting and the tax bases of existing assets and liabilities. To date, we have no history of earnings.

Therefore, our net deferred tax assets are reduced by a valuation allowance to the extent that realization of the related deferred tax asset is not assured.

Basic and Diluted Net Loss Per Common Share

Basic net loss per common share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. The computation of basic net loss per share for all periods presented is derived from the information on the face of the statement of operations, and there are no reconciling items in either the numerator or denominator.

Diluted net loss per common share is computed as though all potential common shares that are dilutive were outstanding during the year, using the treasury stock method for the purposes of calculating the weighted-average number of dilutive common shares outstanding during the period. Potential dilutive common shares consist of shares issuable upon exercise of stock options and warrants. Securities that potentially could have diluted basic earnings per common share, but were excluded from the diluted net loss per common share computation because their inclusion would have been anti-dilutive, were as follows:

	Year Ended December 31,		
	2004	2003	2002
Potential dilutive stock options outstanding	530,731	554,852	796,010
Potential dilutive warrants to purchase common stock outstanding	—	—	242,086
Potential dilutive common shares	530,731	554,852	1,038,096
Outstanding securities excluded from the potential dilutive common shares calculation (1)	3,970,588	4,512,838	3,477,720

(1) For purposes of computing the potential dilutive common shares, we have excluded outstanding stock options and warrants to purchase common stock whose exercise prices exceed the average of the closing sale prices of our common stock as reported on the NASDAQ National Market for the period.

Impairment of Long-Lived Assets

We regularly evaluate our long-lived assets for indicators of possible impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is assessed using discounted cash flows. To date, we have not experienced any such losses.

Reclassifications

We have reclassified certain prior year amounts to conform to our current year's presentation of cash flow used in investing activities for purchases of available-for-sale securities and provided by sales and maturities of available-for-sale securities and our components of gross deferred tax assets in Note 11. These reclassifications had no impact on our financial condition, results of operations, or the net cash flow from investing activities reported on our statement of cash flows.

New Accounting Pronouncements

In March 2004, the Financial Accounting Standards Board (FASB) approved Emerging Issues Task Force (EITF) Issue No. 03-1, *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments."* The objective of this issue is to provide guidance for identifying other-than-temporarily impaired investments. EITF No. 03-1 also provides new disclosure requirements for investments that are deemed to be

temporarily impaired. In September 2004, the FASB issued EITF No. 03-1-1, which delayed the effective date of EITF No. 03-1, with the exception of certain disclosure requirements. We do not believe that the adoption of EITF No. 03-1 will have a material impact on our financial condition and results of operations.

In December 2004, the FASB issued Statement No. 153, ("FAS 153"), *"Exchanges of Nonmonetary Assets, an amendment of APB Opinion No. 29, Accounting for Nonmonetary Transactions."* APB 29 is based on the principle that exchanges of nonmonetary assets should be measured based on the fair value of the assets exchanged. FAS 153 amends APB 29 to eliminate the exception for nonmonetary exchanges of similar productive assets and replaces it with a general exception for exchanges of nonmonetary assets that do not have commercial substance. A nonmonetary exchange has commercial substance if the future cash flows of the entity are expected to change significantly as a result of the exchange. FAS 153 becomes effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. We do not expect the adoption of FAS 153 to have a material impact on our financial position, cash flows, or results of operations.

In December 2004, the FASB issued FASB Statement No. 123(R), ("FAS 123(R)"), *"Share-Based Payment,"* which is a revision of FASB Statement No. 123, *"Accounting for Stock-Based Compensation."* FAS 123(R) supercedes APB Opinion No. 25, (APB 25), *"Accounting for Stock Issued to Employees,"* and amends FASB Statement No. 95, *"Statement of Cash Flows."* FAS 123(R) requires all share-based payments to employees, including grants of employee stock options, to be recognized in the financial statements based on their fair values at the date of grant (i.e., pro forma disclosure is no longer an alternative to financial statement recognition). FAS 123(R) is effective for public companies at the beginning of the first interim or annual period beginning after June 15, 2005. The FASB believes the use of a binomial lattice model for option valuation is capable of more fully reflecting certain characteristics of employee share options compared to the Black-Scholes options pricing model. The new standard may be adopted in one of three ways—the modified prospective transition method, a variation of the modified prospective transition method or the modified retrospective transition method. We are currently evaluating how we will adopt the standard. We do not expect the adoption of FAS 123(R) to have a material impact on our current compensation practices or our statement of cash flows. However, we do expect that our adoption of FAS 123(R) will significantly increase our reported operating expenses which would have a material impact on our results of operations and related financial position for all periods after adoption.

Stock-Based Compensation

We have elected to continue to follow APB 25 and related interpretations, to account for stock options granted to our employees and directors for the year ended December 31, 2004. Under APB 25, using the prescribed intrinsic value method of accounting, no compensation expense is recognized when the exercise price of the stock options equals the market price of the underlying stock on the date of the option grant.

The information regarding net loss and loss per common share as required by FAS 123 has been determined as if we had accounted for our employee stock options under the fair value method prescribed by FAS 123. The resulting effect on net loss and loss per common share pursuant to FAS 123 is not likely to be representative of the effects on net loss and loss per common share pursuant to FAS 123 in future years, since future years are likely to include additional grants and the variable impact of future years' vesting.

The following table illustrates the effect on our net loss and loss per common share if we had applied the fair value recognition provisions of FAS 123 to our stock-based employee compensation (in thousands, except for per share data):

	Year Ended December 31,		
	2004	2003	2002
Net loss—as reported	$(23,923)	$(25,774)	$(27,739)
Add: Stock-based employee compensation included in reported net loss	220	28	—
Less: Total stock-based employee compensation expense determined under the fair- value-based method for all awards...	(6,637)	(9,941)	(12,202)
Net loss—pro forma	$(30,340)	$(35,687)	$(49,941)
Net loss per common share basic and diluted — as reported	$ (1.17)	$ (1.28)	$ (1.38)
Net loss per common share basic and diluted—pro forma	$ (1.49)	$ (1.77)	$ (1.99)

For purposes of disclosure pursuant to FAS 123, as amended by FAS 148, the estimated fair value of our employee stock options is amortized to expense on a straight-line basis over the vesting period of the options, generally over four years. We use the Black-Scholes option valuation model to estimate the fair value of our options on the date of grant. Options that were granted during the years ended December 31, 2004, 2003 and 2002 were valued with the following weighted average assumptions:

	Year Ended December 31,		
	2004	2003	2002
Expected volatility	0.8110	0.8343	1.0459
Risk free interest rate	3.43%	2.97%	4.00%
Expected life of options in years	5	5	5
Expected dividend yield	—	—	—

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options and warrants that have no vesting restrictions and are fully transferable. In addition, option valuation models, including Black-Scholes, require the input of highly subjective assumptions, including the expected stock price volatility. Because our stock options and warrants are not traded, they have characteristics significantly different from those of traded options and warrants, and because changes in the subjective input assumptions can materially affect the fair value estimate, in our opinion, the existing option valuation models, including Black-Scholes, do not necessarily provide a reliable single measure of the fair value of our stock options and warrants.

Our employee stock options are granted at a price equal to the fair market value of our stock on the date of the grant. The weighted-average estimated fair values of stock options granted during the fiscal years ended December 31, 2004, 2003, and 2002 as calculated using the Black-Scholes option pricing model were $2.63, $2.60, and $6.49, respectively.

For equity awards to non-employees, including lenders, lessors, and consultants, we also apply the Black-Scholes method to determine the fair value of such investments in accordance with FAS 123 and Emerging Issues Task Force Issue No. 96-18, *"Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods, or Services."* The options and warrants granted to non-employees are re-measured as they vest and the resulting value is recognized as an expense against our net loss over the period during which the services are received or the term of the related financing.

2. Available-for-Sale Securities

The following is a summary of cash, restricted investments, and available-for-sale securities as of December 31, 2004 (in thousands):

	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash	$ 3,217	$ —	$ —	$ 3,217
Corporate debt securities	33,438	1	(210)	33,229
Federal agency obligations	27,362	—	(248)	27,114
Asset-backed and other securities	3,200	—	(34)	3,166
Short-term municipals	3,350	—	—	3,350
Treasury obligations	6,176	—	(34)	6,142
Total	$76,743	$ 1	$(526)	$76,218
Amounts reported as:				
Cash and cash equivalents	3,217	—	—	3,217
Restricted Investments	11,928	—	—	11,928
Available-for-sale securities	$61,598	$ 1	$(526)	$61,073
Total	$76,743	$ 1	$(526)	$76,218

The weighted average maturity of our investment portfolio at December 31, 2004 was 354 days, with $42.7 million carrying an effective maturity of less than twelve months, and $33.5 million carrying an effective maturity between one and three years.

The following is a summary of cash, restricted investments, and available-for-sale securities as of December 31, 2003 (in thousands):

	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash	$ 2,384	$ —	$ —	$ 2,384
Corporate debt securities	45,474	232	(25)	45,681
Federal agency obligations	24,813	81	(21)	24,873
Asset-backed and other securities	17,048	134	(3)	17,179
Short-term municipals	2,000	—	—	2,000
Treasury obligations	6,757	9	(5)	6,761
Total	$98,476	$456	$(54)	$98,878
Amounts reported as:				
Cash and cash equivalents	2,384	—	—	2,384
Restricted Investments	11,928	—	—	11,928
Available-for-sale securities	$84,164	$456	$(54)	$84,566
Total	$98,476	$456	$(54)	$98,878

The weighted average maturity of our investment portfolio at December 31, 2003 was 405 days, with $46.3 million carrying an effective maturity of less than twelve months, and $52.5 million carrying an effective maturity between one and three years.

Net realized gains were approximately $119,000, $444,000, and $822,000 for the years ended December 31, 2004, 2003, and 2002, respectively.

3. Property and Equipment

Property and equipment consist of the following (in thousands):

	December 31,	
	2004	2003
Leasehold improvements	$ 18,439	$ 18,429
Laboratory equipment	6,930	6,789
Office furniture and equipment	2,301	2,140
	27,670	27,358
Less accumulated depreciation and amortization	(15,173)	(11,717)
Property and equipment, net	$ 12,497	$ 15,641

Total depreciation and amortization expense for the years ended December 31, 2004, 2003 and 2002, was $3.6 million, $3.6 million, and $3.1 million, respectively.

4. Deferred Revenue

In March 2003, we received a $2.5 million payment from Bayer Corporation under the terms of our collaboration agreement for the development of Coagulin-B, our product candidate that we were developing for the treatment of hemophilia B, involving administration to the liver. This amount was recorded as deferred revenue and was being recognized as revenue ratably over the estimated development period for this product, which was determined to be five years, or approximately $125,000 per quarter.

In May 2004, we announced the suspension of subject enrollment in our phase I clinical trial involving the administration of Coagulin-B to the liver. This resulted in the termination of the development of the liver-targeted product candidate associated with the March 2003 Bayer payment. As a result, we accelerated the recognition of the remaining $2.0 million of deferred revenue in our statements of operations during the year ended December 31, 2004.

5. Loan Payable

In June 2000, we entered into a financing arrangement to support construction related activities. Under this arrangement, we had the right to borrow up to $10.0 million through June 1, 2003. This revolving line of credit was amended in June 2002 to extend the expiration date to June 1, 2005, and amended again in June 2004 to extend the expiration date to June 1, 2007. Accordingly, the loan continues to be classified as long term. Amounts borrowed under this arrangement bear interest at the London Inter-Bank Offered Rate plus a margin adjustment that varies between 0.5% and 1.0% on the date of each drawdown based on the market value of our investment portfolio held with a subsidiary of Wells Fargo. This interest rate is subsequently reset every three months. The weighted average interest rate for all outstanding drawdowns on this long-term obligation was 2.70% at December 31, 2004 and 2.75% at December 31, 2003. We have pledged a portion of our portfolio of available-for-sale securities equal to the amount of outstanding borrowings to secure this long-term obligation, and have identified these pledged assets as restricted investments on our balance sheets. As of both December 31, 2004 and 2003, we had borrowed $8.0 million from the line of credit. Payments of interest only are due monthly through June 1, 2007, at which time a balloon payment of outstanding principal is due. In November 2000, we reserved $2.0 million in borrowing capacity from the line of credit to secure a letter of credit. The letter of credit was established pursuant to the terms required under a ten-year property lease entered into in November 2000, and was issued in favor of the property owner. As a result of the cash borrowings and the establishment of the letter of credit, we did not have any remaining borrowing capacity under the line of credit at December 31, 2004.

6. Stockholders' Equity

Common Stock

In August and September 1998, we issued an aggregate of 1,306,505 shares of our common stock at $2.25 to $2.94 per share to selected institutional investors. The offering was completed through a private placement. As part of the transaction, we issued warrants to purchase 261,301 shares of our common stock with an exercise price of $2.18 to $3.67 per share. The exercise price was 125% of the fair market value per share of our underlying stock on the corresponding closing day and the warrants carry a five-year term. After deducting commissions and fees from the gross proceeds of $2,969,000, net proceeds from this transaction approximated $2,735,000.

In December 1998, we issued 1,367,280 shares of our common stock at $3.81 to $4.88 per share to selected institutional investors. The offering was completed through a private placement. As part of this transaction, we issued warrants to purchase 273,456 shares of our common stock with an exercise price ranging from $4.76 to $6.09 per share. The exercise price was 125% of the fair market value per share of our underlying stock on the corresponding closing day and the warrants carry a five-year term. After deducting commissions and fees from the gross proceeds of $5,635,000, net proceeds from this transaction approximated $5,197,000.

In February and April 1999, we issued an aggregate of 2,198,210 shares of our common stock at $5.50 to $6.00 per share to selected institutional investors. The offering was completed through a private placement. As part of this transaction, we issued warrants to purchase 439,642 shares of our common stock with an exercise price of $6.87 to $7.50 per share. The exercise price was 125% of the fair market value per share of the underlying stock on the corresponding closing day and the warrants carry a five-year term. After deducting commissions and fees from the gross proceeds of $13,189,000, net proceeds from this transaction approximated $12,156,000.

In October and November 1999, we issued an aggregate of 2,033,895 shares of our common stock at $16.19 to $25.56 per share to selected institutional investors. The offering was completed through a private placement. As part of this transaction, we issued warrants to purchase 406,779 shares of our common stock with an exercise price of $20.25 to $31.95 per share. The exercise price was 125% of the fair market value per share of our underlying stock on the corresponding closing day and the warrants carry a five-year term. After deducting commissions and fees from the gross proceeds of $40,028,000, net proceeds from this transaction approximated $37,222,000.

In March 2000, we issued a warrant to purchase 40,000 shares of our common stock as partial consideration for the extension of our building lease. The fair value of this warrant at the date of issuance was approximately $1,738,000. This fair value is being amortized over the life of the lease extension. This warrant was issued with an exercise price equal to the fair market value per share of our underlying stock at the time of issuance, or $56.00, and carries a five-year term.

Also, in March 2000, we issued a warrant to purchase 50,000 shares of our common stock as partial consideration for the acquisition of certain patent licenses used in our research and development activities. The fair value of this warrant at the date of issuance was approximately $3,182,000 and was fully expensed in the year ended June 30, 2000. This warrant was issued with an exercise price equal to the fair market value per share of our underlying stock at the time of issuance, or $82.00, and carries a five-year term.

In April and May 2000, we issued an aggregate of 1,150,000 shares of our common stock at $26.00 per share through a public offering. After deducting commissions and fees from the gross proceeds of $29,900,000, net proceeds from this transaction totaled $27,611,000.

In November 2000, we issued an aggregate of 2,291,239 shares of our common stock between $37.50 and $45.06 per share through a public offering. After deducting combined commissions and fees from the gross proceeds of $90,706,000, net proceeds from this transaction totaled $86,086,000.

In February 2001, we issued 313,636 shares of common stock at $47.82 per share to Bayer AG, in connection with a collaboration agreement entered into with Bayer Corporation dated November 17, 2000. Net proceeds from this transaction totaled $15,000,000.

In March 2004, we issued a warrant to purchase 15,000 shares of our common stock as partial consideration for the acquisition of certain intellectual property rights used in our research and development activities. The fair value of this warrant was approximately $97,000 when we entered into the corresponding license agreement in October 2003. The fair value of the warrant was fully expensed and recorded in accounts payable and other accrued liabilities as of December 31, 2003. Upon issuance, the fair value of the warrant was reclassified to additional paid in capital for the year ended December 31, 2004. This warrant was issued with an exercise price equal to the fair market value per share of our underlying stock at the time of issuance, or $6.50, and carries a ten-year term.

At December 31, 2004, we had outstanding warrants to purchase shares of common stock as follows:

Number Of Shares	Exercise Price	Issue Date	Expiration Date
13,324	$ 5.36	1995	2005
4,514	7.09	1995	2005
40,000	56.00	2000	2005
50,000	82.00	2000	2005
15,000	6.50	2004	2013
122,838	$ 5.36 – $82.00		2005 – 2013

Shares Reserved for Future Issuance

We have reserved shares of our common stock for future issuance as follows:

	December 31, 2004
Stock options outstanding	4,424,728
Stock options available for grant	4,390,481
Warrants to purchase common stock	122,838
Shares available for Employee Stock Purchase Plan	360,000
	9,298,047

7. Stock Options and Stock Purchase Plan

Employee Stock Option Plans

Under the 1993 Stock Option Plan (the "1993 Plan"), prior to March 1996, incentive and nonqualified stock options could be granted to our key employees, directors and consultants to purchase up to 1,500,000 shares of common stock. Under the 1993 Plan, options could be granted at a price per share not less than the fair market value at the date of grant. In March 1996, the Board determined to grant no further options under the 1993 Plan and adopted the 1996 Equity Incentive Plan. At December 31, 2004, there were options to purchase 27,844 shares outstanding under the 1993 Plan, with no further shares available for grant.

The 1996 Equity Incentive Plan ("1996 Plan") provides for grants of incentive and nonqualified stock options, restricted stock purchase awards, stock bonuses and stock appreciation rights to our employees, directors and consultants. The Plan originally authorized the grant of options to purchase up to 600,000 shares of common stock. As a result of a series of amendments which were approved by stockholders, prior to December 31, 2004, there were 3,500,000 shares authorized for grant under the 1996 Plan. Under the 1996 Plan, incentive stock options may be granted at a price per share not less than the fair market value at the date of grant, and nonqualified stock options may be granted at a price per share not less than 85% of the fair market value at the date of grant. Options granted generally have a maximum term of 10 years from the grant date and become exercisable over four years. At December 31, 2004, there were options to purchase 1,099,559 shares outstanding under the 1996 Plan and 1,651,239 shares available for grant.

In June 2000, the Board of Directors adopted the 2000 Equity Incentive Plan ("2000 Plan") which provides for grants of nonqualified stock options, restricted stock purchase awards, and stock bonuses to our employees, directors and consultants to purchase up to 5,000,000 shares of common stock; provided, however, that generally only up to 40% of the shares subject to grants under the 2000 Plan may be made to our directors and officers. Under the 2000 Plan, options may be granted at a price per share not less than 85% of the fair market value at the date of grant. Options granted generally have a maximum term of 10 years from the grant date and become exercisable over four years. At December 31, 2004, there were options to purchase 2,539,694 shares outstanding under the 2000 Plan and 2,456,625 shares available for grant.

Employee Stock Purchase Plan

In September 1997, we adopted the 1997 Employee Stock Purchase Plan ("Purchase Plan"). A total of 360,000 shares of our common stock have been reserved for issuance under the Purchase Plan. As of December 31, 2004, there have been no employee contributions to the Purchase Plan.

Non-employee Stock Options

In July 1995, we granted the Chairman of our Board of Directors an option to purchase 515,248 shares of our common stock at $0.49 per share, exercisable for 10 years from the date of grant. At December 31, 2004, the option was fully vested; however, no part of this option had been exercised. Such grant was made outside of any of our stock option plans.

The 1996 Non-Employee Directors' Stock Option Plan (the "Directors' Plan") provides for automatic grants of options to purchase shares of our common stock to our non-employee directors. The Plan originally authorized the grant of options to purchase up to 200,000 shares of common stock. As a result of a series of amendments which were approved by stockholders, prior to December 31, 2004, there were 550,000 shares authorized for grant under the Director's Plan at December 31, 2004. As of December 31, 2004, nonqualified options to purchase approximately 287,383 shares of common stock between $2.00 and $40.75 per share, exercisable for 10 years from the date of grant, have been granted under the Directors' Plan, of which options to purchase 242,383 shares remained outstanding. At December 31, 2004, there were 282,617 shares available for grant under the Directors' Plan.

The following table summarizes option activity with regard to all stock options:

	Outstanding Options	
	Number of Shares	Weighted-Average Exercise Price per Share
Outstanding at December 31, 2001	**4,009,817**	**17.51**
Granted	946,300	8.33
Canceled	(777,002)	24.01
Exercised	(34,627)	3.28
Outstanding at December 31, 2002	**4,144,488**	**14.31**
Granted	685,800	3.73
Canceled	(404,100)	16.21
Exercised	(63,746)	3.81
Outstanding at December 31, 2003	**4,362,442**	**12.62**
Granted	1,111,150	3.92
Canceled	(962,008)	14.63
Exercised	(86,856)	4.63
Outstanding at December 31, 2004	**4,424,728**	**10.16**

The following table summarizes information with regard to total stock options outstanding under all stock option plans at December 31, 2004:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number of Shares	Weighted-Average Remaining Contractual Life	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price
$ 0.49 – $ 0.49	518,634	0.57	$ 0.49	518,634	$ 0.49
0.71 – 3.29	442,333	8.29	$ 2.97	105,899	$ 2.46
3.31 – 3.31	16,900	3.50	$ 3.31	16,900	$ 3.31
3.38 – 3.38	450,000	9.48	$ 3.38	28,124	$ 3.38
3.50 – 3.53	462,657	7.73	$ 3.53	159,316	$ 3.53
3.63 – 6.30	552,032	6.16	$ 5.22	354,606	$ 5.36
6.31 – 8.53	543,900	7.61	$ 7.60	240,015	$ 7.98
8.62 – 14.36	153,015	6.83	$10.74	123,038	$10.80
14.63 – 14.63	595,382	5.38	$14.63	488,588	$14.63
15.44 – 47.63	689,875	4.93	$33.05	685,765	$33.14
$ 0.49 – $47.63	4,424,728	6.11	$10.16	2,720,885	$13.32

The numbers of options exercisable at December 31, 2003 and 2002 were 2,787,690 and 2,192,689, respectively, with a weighted average exercise price of $14.28 and $13.33, respectively.

In March 2004, in connection with the resignation of an executive, we modified the vesting and expiration terms, but did not extend the maximum contractual term, of certain stock options. These modifications resulted in the recognition of $220,000 in non-cash compensation expense during 2004.

In February 2003, in connection with the resignation of two executives, we modified the vesting and expiration terms, but did not extend the maximum contractual term, of certain stock options. These modifications resulted in the recognition of $28,000 in non-cash compensation expense during 2003.

8. Employee Profit Sharing/401(k) Plan

In January 1996, we adopted a Tax Deferred Savings Plan under Section 401(k) of the Internal Revenue Code (the "Plan") for all full-time employees. Under the Plan, our eligible employees can contribute amounts to the Plan via payroll withholding, subject to certain limitations. Our matching contributions to the Plan are discretionary and can only be made in cash. Effective July 1, 2001, we began matching 25% of an employee's contributions up to $2,500 per Plan year. These matching contributions vest ratably over a five-year period based on the employee's initial hire date. Our matching contributions for all employees for the years ended December 31, 2004, 2003 and 2002 were approximately $100,000, $112,000, and $134,000, respectively.

9. Collaboration Agreement

In November 2000, we entered into a collaboration agreement with Bayer Corporation (Bayer) for the development of our Coagulin-B product for the treatment of hemophilia B. Under the terms of the agreement, Bayer, in collaboration with us, would conduct Phase II/III clinical trials for the product and receive exclusive worldwide marketing and distribution rights to the product. In connection with this collaboration agreement, in February 2001, we issued to Bayer AG, an affiliate of Bayer, 313,636 shares of common stock at $47.82 per share, resulting in proceeds of $15 million.

In March 2003, under the terms of the collaboration agreement, we received a $2.5 million payment from Bayer in connection with the ongoing development of Coagulin-B, which is discussed further in Note 1 and Note 4.

In May 2004, we announced a mutual decision to end the phase I clinical trial protocol of Coagulin-B. In August 2004, both parties agreed that Avigen had met all of its contractual obligations required under the collaboration agreement and in December 2004, Bayer terminated the collaboration agreement.

As a result of the termination, Bayer no longer has any financial obligations to finance Phase II/III development of Coagulin-B and all patent and know-how rights licensed to Bayer under the agreement completely revert back to Avigen. Since Avigen was solely responsible for funding the Phase I development, the termination of the agreement has no financial impact on Avigen. In addition, Avigen has the right to develop a product for the treatment of hemophilia B independently or in collaboration with another corporate partner in the future.

10. Commitments

We lease our laboratory, manufacturing, and office facilities and certain equipment under multiple non-cancelable operating lease agreements, which expire at various times through November 2010. Under our two facilities operating leases, we have pledged $2.4 million of our available-for-sale securities to secure letters of credit that serve as deposits that are required under the terms of the leases. Under multiple equipment operating leases, we have pledged $1.5 million of our available-for-sale securities as collateral for the leases. These amounts are included in restricted investments on the balance sheet at December 31, 2004 and 2003. We have the option to purchase the equipment under these operating leases at the greater of their fair value at the end of the lease or 20% of the original cost.

Future minimum lease payments under non-cancelable operating leases are as follows (in thousands):

	Operating Lease
Year ending December 31:	
2005	$ 2,691
2006	2,560
2007	2,543
2008	2,007
2009	1,489
Thereafter	1,262
Total non-cancelable lease payments	$12,552

Rent expense for the years ended December 31, 2004, 2003 and 2002 was $2.6 million, $2.4 million, and $2.3 million, respectively.

We also enter into commitments to fund collaborative research and clinical work performed by third parties. While these contracts are cancelable, we expect the research studies and clinical work to be completed as defined in the terms of the agreements, and all amounts paid when due. At December 31, 2004, the estimated costs related to these commitments totaled approximately $646,000, all of which is expected to be paid within the next twelve to twenty-four months.

11. Income Taxes

Significant components of our deferred tax assets are as follows (in thousands):

	December 31, 2004	December 31, 2003
Net operating loss carryforward	$ 52,500	$ 43,300
Research and development credits	7,400	6,900
Capitalized research and development	6,500	6,300
Depreciation	2,700	2,000
Capitalized patents	800	1,000
Other	1,000	1,400
Gross deferred tax assets	70,900	60,900
Valuation allowance	(70,900)	(60,900)
Net deferred tax assets	$ —	$ —

No provision has been made for income taxes because we have incurred losses since our inception. Deferred income taxes reflect the net tax effects of temporary differences between the carrying value of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Due to our history of losses, a valuation allowance has been provided against the full amount of deferred tax assets due to the uncertainty of realizing any benefits from these assets. The valuation allowance increased by $10,000,000, $11,000,000, and $12,200,000 for the years ended December 31, 2004, 2003 and 2002, respectively.

Deferred tax assets related to carryforwards at December 31, 2004 include approximately $1,400,000 associated with stock option activity for which any subsequently recognized benefits will be credited directly to stockholder's equity.

At December 31, 2004, we had net operating loss carryforwards for federal and state income tax purposes of approximately $149,000,000 and $31,000,000, respectively, which expire in 2005 through 2024. At December 31, 2004, we had research and development credit carryforwards for federal and state income tax purposes of approximately $5,000,000 and $3,600,000, respectively, which expire in 2009 through 2024.

Because of the "change in ownership" provisions of the Internal Revenue Code of 1986, utilization of our tax net operating loss carryforwards and tax credit carryforwards may be subject to an annual limitation in future periods. As a result of the annual limitation, a portion of these carryforwards may expire before ultimately becoming available to reduce future income tax liabilities.

During the preparation of our Notes to the Financial Statements for the year ended December 31, 2004, we determined that our calculation of deferred tax assets for 2003 was underreported, primarily due to the accumulated temporary differences for the recognition of depreciation expense. Accordingly, the amounts reported in the table above for the year ended December 31, 2003 have been revised, resulting in an increase of gross deferred tax assets and offsetting increase in valuation allowance of approximately $1.3 million, respectively. This revision had no effect on our previously reported results of operations or financial condition.

12. Condensed Quarterly Financial Information (Unaudited)

(amounts in thousands except per share data)	Year ended December 31, 2004			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Total revenue	$ 150	$ 2,002	$ 8	$ 35
Net loss	(7,281)	(4,513)	(6,470)	(5,659)
Net loss per share, basic and diluted	(0.36)	(0.22)	(0.32)	(0.27)

(amounts in thousands except per share data)	Year ended December 31, 2003			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Total revenue	$ 30	$ 128	$ 140	$ 165
Net loss	(5,977)	(6,058)	(6,909)	(6,830)
Net loss per share, basic and diluted	(0.30)	(0.30)	(0.34)	(0.34)

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

None.

Item 9A. ***Controls and Procedures***

Evaluation of disclosure controls and procedures. Based on the evaluation as of December 31, 2004, our chief executive officer and chief financial officer have concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Securities Exchange Act of 1934, as amended) were effective to ensure, at a reasonable assurance level, that the information required to be disclosed by us in reports we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and instructions for such reports.

Management's Report on Internal Control over Financial Reporting. Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2004. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control — Integrated Framework.* Our management has concluded that, as of December 31, 2004, our internal control over financial reporting was effective based on these criteria.

Our management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report, a copy of which is included elsewhere herein.

Changes in Internal Control over Financial Reporting. There were no changes in our internal control over financial reporting during the quarter ended December 31, 2004 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Avigen Inc.

We have audited management's assessment, included in the accompanying Management's Report on Internal Controls over Financial Reporting, that Avigen, Inc. 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 (the COSO criteria). Avigen Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, management's assessment that Avigen, Inc. maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Avigen, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Avigen, Inc. as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2004 and the period from inception (October 22, 1998) through December 31, 2004 of Avigen, Inc. and our report dated March 10, 2005 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
March 10, 2005

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

None.

PART III

Item 10. ***Directors and Executive Officers of the Registrant***

The information required by this Item with respect to Executive Officers may be found under the caption, "Executive Officers of the Registrant" at the end of Part I of this Annual Report on Form 10-K. The information required by this Item with respect to Directors, including information with respect to audit committee financial experts, is incorporated herein by reference from the information under the caption, "Proposal 1 — Election of Directors" appearing in the definitive Proxy Statement to be delivered to Avigen's stockholders in connection with the solicitation of proxies for Avigen's 2005 Annual Meeting of Stockholders to be held on May 26, 2005 (the "Proxy Statement").

Section 16(a) Beneficial Ownership Reporting Compliance

The information required by this Item with respect to compliance with Section 16(a) of the Exchange Act is incorporated herein by reference from the section captioned "Section 16(a) Beneficial Ownership Reporting Compliance" contained in the Proxy Statement.

Code of Business Conduct and Ethics

The information required by this Item with respect to our code of ethics is incorporated herein by reference from the section captioned "Proposal 1 — Election of Directors — Code of Business Conduct and Ethics" contained in the Proxy Statement.

Item 11. ***Executive Compensation***

The information required by this Item is set forth in the Proxy Statement under the captions, "Executive Compensation" and "Compensation Committee Interlocks and Insider Participation." Such information is incorporated herein by reference.

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

The information required by this Item with respect to security ownership of certain beneficial owners and management is set forth in the Proxy Statement under the caption, "Security Ownership of Certain Beneficial Owners and Management." Such information is incorporated herein by reference.

The information required by this Item with respect to securities authorized for issuance under our equity compensation plans is set forth in the Proxy Statement under the caption "Proposal 2 — Approval of the Avigen Inc. 2005 Equity Incentive Plan — Equity Compensation Plan Information." Such information is incorporated herein by reference.

Item 13. ***Certain Relationships and Related Transactions***

The information required by this Item is set forth in the Proxy Statement under the heading "Certain Relationships and Related Transactions." Such information is incorporated herein by reference.

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

The information required by this Item is set forth in the Proxy Statement under the heading "Proposal 3 — Ratification of Selection of Independent Registered Public Accounting Firm." Such information is incorporated herein by reference.

Consistent with Section 10A(i)(2) of the Securities Exchange Act of 1934, as added by Section 202 of the Sarbanes-Oxley Act of 2002, we are responsible for listing the non-audit services approved by our Audit Committee to be performed by Ernst & Young LLP, our external auditor. Non-audit services are defined as services other than those provided in connection with an audit or a review of our financial statements. The Audit Committee has not approved, and Ernst & Young LLP has not provided, any non-audit services other than those that Avigen has disclosed in previous SEC filings.

PART IV

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

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

(1) ***Financial Statements:***

Report of Independent Registered Public Accounting Firm
Balance Sheets
Statements of Operations
Statements of Stockholders' Equity
Statements of Cash Flows
Notes to Financial Statements

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

Financial statement schedules have been omitted from this Annual Report on Form 10-K because they are either not applicable or the required information is provided in the financial statements or the notes thereto.

(3) ***Exhibits***

Exhibit Number	Exhibits
3.1(1)	Amended and Restated Certificate of Incorporation
3.1.1(13)	Certificate of Amendment to Certificate of Incorporation
3.2 (1)	Restated Bylaws of the Registrant
4.1(1)	Specimen Common Stock Certificate
10.1(2, 7)	Nonstatutory Stock Option Outside of Plans to Philip J. Whitcome
10.2(1, 2)	1993 Stock Option Plan
10.3 (2, 17)	1996 Equity Incentive Plan, as amended
10.4(1, 2)	Form of Incentive Stock Option Grant for 1996 Equity Incentive Plan
10.5(1, 2)	Form of Nonstatutory Stock Option Grant for 1996 Equity Incentive Plan
10.6(2, 14)	1996 Non-Employee Directors' Stock Option Plan, as amended
10.7(2, 4)	1997 Employee Stock Purchase Plan
10.8(1, 2)	Form of Indemnification Agreement between Avigen and its directors and executive officers.
10.9(1)	Form of Common Stock Warrant
10.10(2, 5)	2000 Equity Incentive Plan
10.11(2, 12)	Form of Nonstatutory Stock Option Grant for 2000 Equity Incentive Plan
10.14(2, 15)	Form of Incentive Stock Option Grant for 1993 Stock Option Plan
10.15(2, 15)	Form of Nonstatutory Stock Option Grant for 1993 Stock Option Plan
10.16(2)	Form of Nonstatutory Stock Option Grant for 1996 Non-Employee Directors' Stock Option Plan, as amended
10.17(2)	Compensation Agreements with Named Executive Officers
10.27(1,2)	Employment Agreement dated August 10, 1992, between Avigen and John Monahan
10.29(2, 6)	Employment Agreement dated August 14, 1996, between Avigen and Thomas J. Paulson
10.32(15)	Revolving line of credit note signed November 2, 2000 with Wells Fargo Bank
10.33(15)	Letter Agreement to the revolving line of credit note signed November 2, 2000 with Wells Fargo Bank.
10.36(2, 8)	Management Transition Plan
10.38(4, 11)	Factor IX patent and Know-How Exclusive License Agreement Between The Children's Hospital of Philadelphia and Avigen, dated May 20, 1999.
10.39(9, 11)	License Agreement between Avigen and the University of Florida Research Foundation, Inc., dated November 13, 1992, and its First Amendment, dated March 25, 1996.
10.41(10)	Property Lease Agreement between ARE-1201 Harbor Bay, LLC and Avigen, dated February 29, 2000
10.45(13)	Office Lease Agreement between Lincoln-RECP Empire OPCO, LLC and Avigen, Inc., dated November 2, 2000.
10.46(13)	First Amendment to Lease Agreement between Lincoln-RECP Empire OPCO, LLC and Avigen, Inc., dated December 1, 2000.

Exhibit Number	Exhibits
10.47(13)	Second Amendment to Lease Agreement between Lincoln-RECP Empire OPCO, LLC and Avigen, Inc., dated February 12, 2001.
10.49(16)	Revolving line of credit note with Wells Fargo Bank, dated June 1, 2002.
10.50(16)	Letter of Agreement to the revolving line of credit note signed June 1, 2002 with Wells Fargo Bank.
10.51(11, 23)	License Agreement, dated November 21, 2003, by and between University of Colorado and Avigen
10.52 (2, 22)	Separation Agreement dated March 8, 2004 between Avigen and John Monahan
10.53 (20)	Revolving line of credit note with Wells Fargo Bank, dated June 1, 2004
10.54 (20)	Amendment to Letter of Agreement to the revolving line of credit note signed June 1, 2004 with Wells Fargo Bank
10.55 (2, 21)	Arrangement Regarding Non-Employee Director Compensation
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (included on the signature pages hereto)
31.1	CEO Certification required by Rule 13a-14(a) or Rule 15d-14(a)
31.2	CFO Certification required by Rule 13a-14(a) or Rule 15d-14(a)
32.1(19)	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350)

Keys to Exhibits:

(1) Filed as an exhibit to the Registrant's Registration Statement on Form S-1 (No. 333-03220) and incorporated herein by reference.

(2) Management Contract or Compensation Plan.

(4) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 1999, as filed with the SEC (Commission File No. 000-28272).

(5) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-42210) filed with the SEC on July 25, 2000.

(6) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 1997, as filed with the SEC (Commission File No. 000-28272).

(7) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-12087) filed with the SEC on September 16, 1996.

(8) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended September 30, 1998, as filed with the SEC (Commission File No. 000-28272).

(9) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K/A for the year ended June 30, 1999, as filed with the SEC (Commission File No. 000-28272).

(10) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended March 31, 2000, as filed with the SEC (Commission File No. 000-28272).

(11) Portions of this exhibit have been omitted pursuant to a grant of confidential treatment.

(12) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 2000, as filed with the SEC on September 27, 2000 (Commission File No. 000-28272).

(13) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended December 31, 2000, as filed with the SEC (Commission File No. 000-28272).

(14) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-56274) filed with the SEC on June 22, 2004.

(15) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 2001, as filed with the SEC on September 27, 2001 (Commission File No. 000-28272).

(16) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended June 30, 2002, as filed with the SEC (Commission File No. 000-28272).

(17) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-90504) filed with the SEC on June 14, 2002.

(19) his certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Avigen under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

(20) ncorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended June 30, 2004, as filed with the SEC (Commission File No. 000-28272).

(21) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004, as filed with the SEC (Commission File No. 000-28272).

(22) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004, as filed with the SEC (Commission File No. 000-28272).

(23) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended December 31, 2003, as filed with the SEC on March 15, 2004 (Commission File No. 000-28272).

SIGNATURES

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

AVIGEN, INC.

By: /s/ KENNETH G. CHAHINE
Kenneth G. Chahine, Ph.D.
President and Chief Executive Officer

Dated: March 10, 2005

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Kenneth Chahine and Philip J. Whitcome, and each or any one of them, his true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Kenneth G. Chahine Kenneth G. Chahine, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2005
/s/ Thomas J. Paulson Thomas J. Paulson	Chief Financial Officer (Principal Financial and Accounting Officer)	March 10, 2005
/s/ Philip J. Whitcome Philip J. Whitcome, Ph.D.	Chairman of the Board	March 10, 2005
/s/ Zola Horovitz Zola Horovitz, Ph.D.	Director	March 10, 2005
/s/ Yuichi Iwaki Yuichi Iwaki, M.D., Ph.D.	Director	March 10, 2005
/s/ John K.A. Prendergast John K.A. Prendergast, Ph.D.	Director	March 10, 2005
/s/ Daniel Vapnek Daniel Vapnek, Ph.D.	Director	March 10, 2005

EXHIBIT INDEX

Exhibit Number	Exhibits
3.1(1)	Amended and Restated Certificate of Incorporation
3.1.1(13)	Certificate of Amendment to Certificate of Incorporation
3.2 (1)	Restated Bylaws of the Registrant
4.1(1)	Specimen Common Stock Certificate
10.1(2, 7)	Nonstatutory Stock Option Outside of Plans to Philip J. Whitcome
10.2(1, 2)	1993 Stock Option Plan
10.3 (2, 17)	1996 Equity Incentive Plan, as amended
10.4(1, 2)	Form of Incentive Stock Option Grant for 1996 Equity Incentive Plan
10.5(1, 2)	Form of Nonstatutory Stock Option Grant for 1996 Equity Incentive Plan
10.6(2, 14)	1996 Non-Employee Directors' Stock Option Plan, as amended
10.7(2, 4)	1997 Employee Stock Purchase Plan
10.8(1, 2)	Form of Indemnification Agreement between Avigen and its directors and executive officers.
10.9(1)	Form of Common Stock Warrant
10.10(2, 5)	2000 Equity Incentive Plan
10.11(2, 12)	Form of Nonstatutory Stock Option Grant for 2000 Equity Incentive Plan
10.14(2, 15)	Form of Incentive Stock Option Grant for 1993 Stock Option Plan
10.15(2, 15)	Form of Nonstatutory Stock Option Grant for 1993 Stock Option Plan
10.16(2)	Form of Nonstatutory Stock Option Grant for 1996 Non-Employee Directors' Stock Option Plan, as amended
10.17(2)	Compensation Agreements with Named Executive Officers
10.27(1, 2)	Employment Agreement dated August 10, 1992, between Avigen and John Monahan
10.29(2, 6)	Employment Agreement dated August 14, 1996, between Avigen and Thomas J. Paulson
10.32(15)	Revolving line of credit note signed November 2, 2000 with Wells Fargo Bank
10.33(15)	Letter Agreement to the revolving line of credit note signed November 2, 2000 with Wells Fargo Bank
10.36(2, 8)	Management Transition Plan
10.38(4, 11)	Factor IX patent and Know-How Exclusive License Agreement Between The Children's Hospital of Philadelphia and Avigen, dated May 20, 1999
10.39(9, 11)	License Agreement between Avigen and the University of Florida Research Foundation, Inc., dated November 13, 1992, and its First Amendment, dated March 25, 1996
10.41(10)	Property Lease Agreement between ARE-1201 Harbor Bay, LLC and Avigen, dated February 29, 2000
10.45(13)	Office Lease Agreement between Lincoln-RECP Empire OPCO, LLC and Avigen, Inc., dated November 2, 2000
10.46(13)	First Amendment to Lease Agreement between Lincoln-RECP Empire OPCO, LLC and Avigen, Inc., dated December 1, 2000

Exhibit Number	Exhibits
10.47(13)	Second Amendment to Lease Agreement between Lincoln-RECP Empire OPCO, LLC and Avigen, Inc., dated February 12, 2001.
10.49(16)	Revolving line of credit note with Wells Fargo Bank, dated June 1, 2002.
10.50(16)	Letter of Agreement to the revolving line of credit note signed June 1, 2002 with Wells Fargo Bank.
10.51(11, 23)	License Agreement, dated November 21, 2003, by and between University of Colorado and Avigen
10.52 (2, 22)	Separation Agreement dated March 8, 2004 between Avigen and John Monahan
10.53 (20)	Revolving line of credit note with Wells Fargo Bank, dated June 1, 2004
10.54 (20)	Amendment to Letter of Agreement to the revolving line of credit note signed June 1, 2004 with Wells Fargo Bank
10.55 (2, 21)	Arrangement Regarding Non-Employee Director Compensation
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (included on the signature pages hereto)
31.1	CEO Certification required by Rule 13a-14(a) or Rule 15d-14(a)
31.2	CFO Certification required by Rule 13a-14(a) or Rule 15d-14(a)
32.1(19)	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350)

Keys to Exhibits:

(1) Filed as an exhibit to the Registrant's Registration Statement on Form S-1 (No. 333-03220) and incorporated herein by reference.

(2) Management Contract or Compensation Plan.

(4) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 1999, as filed with the SEC (Commission File No. 000-28272).

(5) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-42210) filed with the SEC on July 25, 2000.

(6) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 1997, as filed with the SEC (Commission File No. 000-28272).

(7) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-12087) filed with the SEC on September 16, 1996.

(8) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended September 30, 1998, as filed with the SEC (Commission File No. 000-28272).

(9) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K/A for the year ended June 30, 1999, as filed with the SEC (Commission File No. 000-28272).

(10) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended March 31, 2000, as filed with the SEC (Commission File No. 000-28272).

(11) Portions of this exhibit have been omitted pursuant to a grant of confidential treatment.

(12) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 2000, as filed with the SEC on September 27, 2000 (Commission File No. 000-28272).

(13) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended December 31, 2000, as filed with the SEC (Commission File No. 000-28272).

(14) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-56274) filed with the SEC on June 22, 2004.

(15) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended June 30, 2001, as filed with the SEC on September 27, 2001 (Commission File No. 000-28272).

(16) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended June 30, 2002, as filed with the SEC (Commission File No. 000-28272).

(17) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Registration Statement on Form S-8 (Registration No. 333-90504) filed with the SEC on June 14, 2002.

(19) This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Avigen under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

(20) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended June 30, 2004, as filed with the SEC (Commission File No. 000-28272).

(21) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004, as filed with the SEC (Commission File No. 000-28272).

(22) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004, as filed with the SEC (Commission File No. 000-28272).

(23) Incorporated by reference from such document filed with the SEC as an exhibit to Avigen's Annual Report on Form 10-K for the year ended December 31, 2003, as filed with the SEC on March 15, 2004 (Commission File No. 000-28272).

Exhibit 23.1

CONSENT OF INDEPENDENT PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements on Form S-8 (Reg. Nos. 333-12087, 333-68637, 333-94111, 333-42210, 333-56274, 333-90504 and 333-116740) pertaining to the 1993 Stock Option Plan, the Non-Statutory Stock Option, the 1996 Equity Incentive Plan, the 1996 Non-Employee Directors' Stock Option Plan, the 1997 Employee Stock Purchase Plan, and the 2000 Equity Incentive Plan, and Registration Statements on Form S-3 (Reg. Nos. 333-68117, 333-72225, 333-79925, 333-92355 and 333-47680) and in the related Prospectuses of Avigen, Inc. of our reports dated March 10, 2005, with respect to the financial statements of Avigen, Inc., Avigen, Inc. management's assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of Avigen, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2004.

/s/ ERNST & YOUNG LLP

Palo Alto, California
March 10, 2005

EXHIBIT 31.1

CERTIFICATION

I, Kenneth Chahine, certify that:

1. I have reviewed this Annual Report on Form 10-K of Avigen, 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 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 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 10, 2005

/s/ KENNETH G. CHAHINE

Kenneth G. Chahine
Chief Executive Officer and President
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION

I, Thomas J. Paulson, certify that:

1. I have reviewed this Annual Report on Form 10-K of Avigen, 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 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 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 10, 2005

/s/ THOMAS J. PAULSON

Thomas J. Paulson
Vice President, Finance,
Chief Financial and Accounting Officer, and
Secretary (Principal Financial Officer)

EXHIBIT 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Kenneth Chahine, Chief Executive Officer of Avigen, Inc. (the "Company"), and Thomas J. Paulson, Chief Financial Officer of the Company, each hereby certify that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2004, and to which this Certification is attached as Exhibit 32.1, (the "Periodic Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

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

In Witness Whereof, the undersigned have set their hands hereto as of the 10th day of March, 2005.

/s/ KENNETH G. CHAHINE

Kenneth G. Chahine
Chief Executive Officer

/s/ THOMAS J. PAULSON

Thomas J. Paulson
Chief Financial Officer

Board of Directors and Senior Management

BOARD OF DIRECTORS

Philip J. Whitcome, Ph.D.
Chairman of the Board

John K. A. Prendergast, Ph.D. *(1, 2, 3)*
Lead Independent Director
President, SummerCloud Bay, Inc.

Yuichi Iwaki, M.D., Ph.D. *(1, 2)*
Professor of Urology,
Pathology and Surgery,
Director of Transplantation Immunology,
University of Southern California School of Medicine

Kenneth G. Chahine, Ph.D., J.D.
President, Chief Executive Officer

Zola Horovitz, Ph.D. *(1, 2, 3)*
Pharmaceutical Consultant,
Former Vice President,
Business Development & Planning,
Bristol-Myers Squibb Co.

Daniel Vapnek, Ph.D. *(1, 3)*
Adjunct Professor,
University of California,
Santa Barbara
Former Senior Vice President of Research, Amgen, Inc.

(1) Governance and Nominating Committee (2) Audit Committee (3) Compensation Committee

OFFICERS

Philip J. Whitcome, Ph.D.
Chairman of the Board

Thomas J. Paulson
Chief Financial Officer

Dawn McGuire, M.D.
Chief Medical Officer

Kirk Johnson, Ph.D.
Vice President,
Preclinical Development

Kenneth G. Chahine, Ph.D., J.D.
President, Chief Executive Officer

Glenn Pierce, M.D., Ph.D.
Vice President, Research and Clinical Development

Michael Coffee
Chief Business Officer

Christina Thomson, J.D.
Vice President, Corporate Counsel

Corporate Information

CORPORATE HEADQUARTERS

1301 Harbor Bay Parkway
Alameda, California 94502
510-748-7150 Telephone
510-748-7155 Facsimile
www.avigen.com

LEGAL COUNSEL

Cooley Godward LLP
Palo Alto, California

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Ernst & Young LLP
Palo Alto, California

TRANSFER AGENT & REGISTRAR

Stockholders with questions regarding stock transfer requirements, lost certificates, and changes of address should contact our Transfer Agent:

American Stock
Transfer & Trust Co.
59 Maiden Lane
New York, New York 10038
1-800-937-5449

INVESTOR RELATIONS

For additional information about Avigen, please see our web page at www.avigen.com. Investor inquiries and requests for additional copies of this report, free of charge, should be directed to Investor Relations at 510-748-7150 or via e-mail at ir@avigen.com.

COMMON STOCK INFORMATION

The Company's common stock is traded on the Nasdaq National Market under the symbol AVGN. As of March 1, 2005 there were approximately 140 stockholders of record of the Company's common stock and 20,381,250 shares of common stock outstanding.

Avigen has not paid dividends on its common stock since the Company's inception, and does not anticipate paying any dividends in the foreseeable future.

ANNUAL MEETING

The annual meeting of stockholders will be held on Thursday, May 26, 2005, at 10:00 a.m. PDT, at Avigen's corporate headquarters, 1301 Harbor Bay Parkway Alameda, California 94502.

STOCKHOLDER COMMUNICATIONS WITH THE BOARD OF DIRECTORS

Stockholders who wish to communicate with the Board or an individual director may send a written communication addressed as follows:

Avigen Board Communication
1301 Harbor Bay Parkway
Alameda, California 94502

Or send by e-mail to: board@avigen.com

AVIGEN

1301 Harbor Bay Parkway
Alameda, CA 94502
510-748-7150 phone
510-748-7155 fax
www.avigen.com