

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

FORM 10-K

/ X / Annual Report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

For the fiscal year ended DECEMBER 31, 1999, or

/ / Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

For the transition period from \_\_\_\_\_ to \_\_\_\_\_.

Commission file number: 0-21088

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

DELAWARE  
(State or other jurisdiction of incorporation or organization) 93-0948554  
(IRS Employer Identification No.)

9373 TOWNE CENTRE DRIVE, SUITE 100, SAN DIEGO, CA 92121-3088  
Address of principal executive offices

(858) 646-1100  
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, Par Value \$0.01  
Preferred Stock Purchase Rights,  
Par Value \$0.01 (Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes X No  
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Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [X]

The aggregate market value of the Common Stock held by non-affiliates of the registrant, based upon the last sale price of the Common Stock reported on the National Association of Securities Dealers Automated Quotation National Market System on March 15, 2000, was \$560,514,000.

The number of shares of Common Stock outstanding as of March 15, 2000, was 19,814,986.

DOCUMENTS INCORPORATED BY REFERENCE

(To the Extent Indicated Herein)

Registrant's Proxy Statement to be filed with the Securities and Exchange Commission in connection with the solicitation of proxies for the Registrant's 2000 Annual Meeting of Stockholders to be held on May 18, 2000, is incorporated by reference in Part III, Items 10 (as to directors), 11, 12 and 13 of this Form 10-K.

FORWARD-LOOKING STATEMENTS

The statements incorporated by reference or contained in this report discuss our future expectations, contain projections of our results of operations or financial condition, and include other "forward-looking" information within the meaning of Section 27A of the Securities Act of 1933, as amended. Our actual results may differ materially from those expressed in forward-looking statements made or incorporated by reference in this report. Forward-looking statements that express our beliefs, plans, objectives, assumptions or future events or performance may involve estimates, assumptions, risks and uncertainties. Therefore, our actual results and performance may differ materially from those expressed in the forward-looking statements. Forward-looking statements often, although not always, include words or phrases such as the following:

- "will likely result,"
- "are expected to,"
- "will continue,"
- "is anticipated,"
- "estimate,"
- "intends,"
- "plans,"
- "projection," and
- "outlook."

You should not unduly rely on forward-looking statements contained or incorporated by reference in this report. Actual results or outcomes may differ materially from those predicted in our forward-looking statements due to the risks and uncertainties inherent in our business, including risks and uncertainties in:

- clinical trial results,
- obtaining and maintaining regulatory approval,
- market acceptance of and continuing demand for our products,
- the attainment of patent protection for any of these products,
- the impact of competitive products, pricing and reimbursement policies,
- our ability to obtain additional financing to support our operations,
- the continuation of our corporate collaborations, and
- changing market conditions and other risks detailed below.

You should read and interpret any forward-looking statements together with the following documents:

- our Quarterly Reports on Form 10-Q,
- the risk factors contained in this report under the caption "Risk Factors," and
- our other filings with the Securities and Exchange Commission.

Any forward-looking statement speaks only as of the date on which that statement is made. We will not update any forward-looking statement to reflect events or circumstances that occur after the date on which such statement is made.

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## PART I

### ITEM 1. BUSINESS

#### OVERVIEW

We develop biopharmaceutical products based on our patented naked DNA gene transfer technologies for the prevention and treatment of life-threatening diseases. We currently focus our development on innovative cancer therapies to induce an immune response against cancer cells without causing serious side effects. We have retained all rights to our internally developed cancer product candidates. Our lead immunotherapy product candidate, ALLOVECTIN-7, is in Phase III and Phase II registration trials for patients with advanced metastatic malignant melanoma, an aggressive form of skin cancer, and in a Phase II clinical trial for patients with persistent or recurrent cancer of the head and neck. Our second immunotherapy product candidate, LEUVECTIN, is in Phase II clinical trials for patients with advanced metastatic kidney cancer and for high-risk patients with locally confined prostate cancer. VAXID, a cancer vaccine intended to prevent recurrence of low-grade, non-Hodgkin's B-cell lymphoma, is in a Phase I/II clinical trial. We are supporting clinical testing of a cancer vaccine for the treatment of advanced metastatic melanoma in a collaboration with the National Cancer Institute, NCI.

We enter into collaborations with major pharmaceutical companies to leverage our technologies primarily for non-cancer applications such as vaccines for infectious diseases and optimized delivery of therapeutic proteins. We have established relationships through the license of our technology with a growing number of corporate partners and collaborators

including:

- - Merck and Co., Inc.,
- - Two divisions of Aventis S.A., formerly Rhone-Poulenc S.A.,
  - - Aventis Pasteur, formerly Pasteur Merieux Connaught,
  - - Aventis Pharma, formerly Rhone-Poulenc Rorer Pharmaceuticals, Inc.,
- - Pfizer Inc,
- - Merial, the animal health joint venture between Merck and Rhone Merieux,
- - Centocor, a wholly-owned subsidiary of Johnson & Johnson,
- - Boston Scientific Corporation.
- - Human Genome Sciences, Inc., and Vascular Genetics Inc.

#### HISTORICAL APPROACHES TO GENE DELIVERY

A typical living cell in the body contains thousands of different proteins essential to cellular structure, growth, and function. Proteins are produced by the cell according to a set of genetic instructions encoded by DNA, which contains all the information necessary to control the cell's biological processes.

DNA is organized into segments called genes, with each gene containing the information required to produce a specific protein. Production of the protein encoded by a particular gene is known as gene expression. The improper expression of even a single gene can severely alter a cell's normal function, frequently resulting in a disease. Gene delivery is an approach to the treatment and prevention of diseases in which genes are introduced into cells to direct the production of specific proteins which have a desired biological effect.

Historically, gene delivery was accomplished by inserting the desired gene into a delivery vehicle, or vector. The most common vectors were viruses that had been genetically disabled so that they could not reproduce and infect other cells. Gene delivery approaches using viruses suffer several drawbacks that may limit their widespread usefulness, including adverse immune responses and inflammation that may inhibit the activity of the virus-based therapy and prevent repeated administration. In addition, viruses can induce permanent changes in the patient's genetic makeup, which may lead to cancer. Some gene delivery product candidates under development at competing companies use viral vectors, but many of the newer formulations are using non-viral or synthetic vectors such as lipids or polymers.

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#### OUR NAKED DNA TECHNOLOGY

The key discovery leading to our patented naked DNA direct gene delivery technology was that some muscle tissues can absorb genetic material directly, without the use of viral components, and subsequently express a desired protein for periods ranging from weeks to several months. Our naked DNA gene delivery approach involves the design and construction of plasmids, DNA segments whose ends are attached together to form a highly stable closed loop. These plasmids contain the gene encoding the protein of interest as well as short segments of DNA that control the rate and location of protein expression. Plasmids can be manufactured through conventional fermentation and purification techniques. Since the initial discovery of the naked DNA technology, our researchers have improved the design of our plasmids to provide dramatic increases in efficiency of gene delivery and expression. In addition, we are developing other synthetic technologies to deliver DNA directly into some non-muscle tissues, including the use of lipid molecules that facilitate direct absorption of DNA into cells.

A narrow definition of "naked DNA" includes only pure plasmid DNA. A broader definition includes plasmid DNA formulated with agents such as lipids or polymers. We call ourselves "The Naked DNA Company-(TM)-" because all of our product candidates are based on these synthetic, non-viral gene delivery methods, and because we own exclusive, broad rights to the naked DNA gene delivery technologies through our series of core patents.

Our naked DNA gene delivery approach may offer novel treatment alternatives for diseases that are currently poorly addressed. Benefits of our gene delivery technology may include:

- - BROAD APPLICABILITY. Our naked DNA gene delivery technology may be useful in developing novel treatments for cancer, DNA vaccines to prevent or treat infectious diseases and methods to efficiently deliver human and animal therapeutic proteins.
- - CONVENIENCE. Our naked DNA therapeutics are intended to be administered like conventional pharmaceuticals on an outpatient basis.
- - SAFETY. Our product candidates contain no viral components which may cause unwanted immune responses, infections, or malignant and permanent changes in

the cell's genetic makeup.

- - EASE OF MANUFACTURING. Our product candidates are manufactured using conventional fermentation techniques and standard purification procedures.
- - COST-EFFECTIVENESS. Our naked DNA gene delivery technology may prove to be more cost-effective than therapies which require genetic modification and controlled propagation of viral vectors. The DNA, once introduced into the body, is intended to stimulate the production of a therapeutic protein over a prolonged period of time, which may be more cost-effective than administering the protein itself.

Potential applications of our naked DNA gene delivery technology include DNA therapeutics for cancer, in which the expressed protein is an immune system stimulant or cancer-killing agent, DNA vaccines for infectious diseases, in which the expressed protein is an antigen, and DNA therapeutic protein delivery, in which the expressed protein is a therapeutic agent.

#### BUSINESS STRATEGY

There are three basic elements to our business strategy:

##### INDEPENDENTLY DEVELOP CANCER THERAPEUTICS

We currently focus our resources on the independent development of cancer therapeutics. The large and rapidly growing market for cancer products is poorly addressed by existing treatment alternatives. In addition, this market is well-suited to a development-stage company with limited resources such as Vical because:

- - Clinical testing usually can be conducted in a small number of patients and benefits can be detected and verified in reasonably short periods of time,
- - Testing occurs in patients with advanced, life-threatening diseases with limited treatment alternatives, which may expedite the regulatory approval process,

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- - Product acceptance is driven by objective clinical data, potentially reducing marketing costs, and
- - Treatment decisions are made at regional cancer centers by oncologists who can be served by a small, specialized sales force.

We intend to retain significant participation in the commercialization of our proprietary cancer products, although we may choose to enlist the support of a marketing partner to accelerate market penetration.

##### EXPAND THE APPLICATIONS OF OUR TECHNOLOGY THROUGH STRATEGIC COLLABORATIONS

Our naked DNA technology can potentially be applied to the treatment or prevention of a wide range of diseases in addition to cancer. In markets that would require large-scale development, high-capacity manufacturing or mass marketing, we have chosen to establish partnerships with major pharmaceutical companies. These companies have the resources necessary to develop and commercialize products for these markets. The resulting collaborations typically provide us with upfront and milestone payments during product development, as well as the potential for ongoing royalties from product sales. Our collaborations to date have involved multiple applications for DNA vaccines and DNA therapeutic protein delivery.

##### DEVELOP FUTURE PRODUCT OPPORTUNITIES

We are actively pursuing the development of future products, refinement of our plasmids and lipids, the exploration of alternative gene delivery technologies, and the evaluation of potential enhancements to our core naked DNA technologies. We also seek and develop additional applications of our technologies by testing new approaches to disease control or prevention. These efforts could lead to further independent product development or to additional licensing opportunities. In addition, we continually evaluate compatible technologies or products that may be of potential interest for in-licensing or acquisition.

#### PRODUCT DEVELOPMENT

The following table summarizes the status of our independent and collaborative product development programs and identifies corporate partners where relevant.

In the table below:

- - "Research" indicates research related to identification and synthesis of lead compounds.
- - "Preclinical" indicates that a specific compound is undergoing toxicology testing and manufacturing scale-up, among other things, in preparation for filing an application for an Investigational New Drug, IND.

In Phase I, trials are conducted with a small number of healthy volunteers to determine the safety profile, the pattern of drug distribution and metabolism. In Phase II, trials are conducted with a larger group of patients afflicted with a target disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety. In the case of products for life-threatening diseases, the initial human testing is generally done in patients rather than in healthy volunteers. Since these patients are already afflicted with the target disease, it is possible that these studies may provide results traditionally obtained in Phase II trials. Such trials are frequently referred to as "Phase I/II" trials. In Phase III, large scale, multi-center, comparative trials are conducted with patients afflicted with a target disease in order to provide enough data for the statistical proof of safety and efficacy required by the FDA and other regulatory authorities.

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PROJECT ----- <S>	TARGET INDICATION(S) ----- <C>	DEVELOPMENT STATUS ----- <C>	DEVELOPMENT RIGHTS ----- <C>
CANCER			
ALLOVECTIN-7	Melanoma, Head and neck cancer	Phase III Phase II	Vical Vical
LEUVECTIN	Renal cell carcinoma Prostate cancer	Phase II Phase II	Vical Vical
VAXID	B-cell lymphoma	Phase I/II	Vical
gp100	Melanoma	Phase I/II	Vical
Therapeutic DNA vaccines	Various cancers	Preclinical/Phase I	Centocor
INFECTIOUS DISEASES			
Preventive DNA vaccines	Influenza, human immunodeficiency virus	Phase I	Merck
	Malaria	Phase I	Aventis Pasteur, formerly Pasteur Merieux Connaught
	Hepatitis B, hepatitis C, human immunodeficiency virus, human papilloma virus, herpes simplex, tuberculosis	Research/preclinical	Merck
Therapeutic DNA vaccines	CMV, H. pylori, Lyme, RSV, varicella zoster	Research/preclinical	Aventis Pasteur, formerly Pasteur Merieux Connaught
	Hepatitis B, human immunodeficiency virus, human papilloma virus	Research/preclinical	Merck
OTHER DISEASES			
Therapeutic protein DNA	Neurodegenerative diseases	Research/preclinical	Aventis Pharma, formerly Rhone-Poulenc Rorer
Catheter-based DNA therapy	Cardiovascular diseases	Research/preclinical	Boston Scientific
VETERINARY			
Preventive DNA vaccines	Various	Research	Merial
Therapeutic protein DNA	Various	Research	Pfizer

#### DNA THERAPEUTICS FOR CANCER

Cancer is a group of diseases in which certain cells grow uncontrolled by the body's normal self-regulatory mechanisms. Surgery is the most effective therapy for locally confined cancers. But surgery is not practical or curative for invasive or metastatic disease that has spread beyond a few locations. Radiation therapy can shrink or eliminate individual tumors, but cannot effectively treat widespread metastases. In addition, high

doses of radiation can destroy the healthy underlying tissue. Chemotherapy seeks to control cancer by killing rapidly dividing cells. However, a number of non-malignant cells in the body, such as bone marrow cells, also rapidly divide and are highly susceptible to chemotherapy. Thus, doses sufficient to eradicate the cancer often cause life-threatening side effects. None of these conventional approaches can eliminate all cancer cells in advanced disease, so recurrence after treatment is common.

A therapeutic approach that selectively kills tumor cells would be far superior to currently available therapies. One approach would be to generate a specific immune response targeting cancer cells without damaging other normal tissues. It is generally believed that the immune system can selectively recognize cancer cells as abnormal and destroy them. However, the vast majority of cancers arise spontaneously in patients with an otherwise normal immune system. This observation suggests that cancer cells somehow escape the normal immune defense mechanisms or that the killer T-cell response produced by cancer patients is not powerful enough to kill all of the abnormal cells. A variety of methods can augment the

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immune response against tumor cells, including the systemic administration of natural immune-enhancing proteins such as interleukin-2, IL-2, and interferon-alpha either alone or in combination with other agents. These methods have shown encouraging results in some patients with some tumor types. However, systemic administration of these agents requires large and frequent doses that also cause serious side effects.

Our scientists are developing novel gene-based cancer immunotherapies to address the shortcomings of existing therapies. These immunotherapeutic product candidates are summarized below.

#### ALLOVECTIN-7

ALLOVECTIN-7 is a DNA/lipid complex containing the human gene encoding HLA-B7 antigen which is found infrequently in the human population. ALLOVECTIN-7 is designed to be injected directly into a tumor, where malignant cells absorb it and express the HLA-B7 antigen. This antigen alerts the immune system to the presence of foreign tissue, inducing the type of powerful immune response seen in organ transplant rejection. In addition, the treatment may trigger an immune response against additional tumor cells, both locally and systemically, by enabling the immune system to recognize other features of the tumor cells. ALLOVECTIN-7 is currently in advanced clinical testing for patients with metastatic melanoma and for patients with persistent or recurrent tumors of the head and neck.

#### METASTATIC MELANOMA

Melanoma is a skin cancer found predominantly in Caucasians, particularly in fair-skinned individuals who have experienced repeated sunburn. According to American Cancer Society, ACS, statistics, 44,200 new cases of melanoma will be diagnosed in the U.S. and 7,300 patients will die from this disease in 1999. NCI estimates that about 480,000 Americans currently suffer from malignant melanoma. If detected when the disease is still limited to one site, known as stage I and II, melanoma usually can be treated successfully by surgery. If untreated, the disease frequently spreads to the lymph glands, lungs, liver, brain and other organs. Stage III is defined as metastatic disease limited to one region and is treated with a combination of surgery and chemotherapy. Stage IV disease involves advanced regional or any distant tumors and treatment normally includes some combination of chemotherapy, radiotherapy, and surgery. The five-year survival of patients with stage III and stage IV disease is 59 percent and 12 percent, respectively. In patients whose disease continues to progress after they have received all available treatments, the average survival is seven to nine months.

We believe ALLOVECTIN-7 will provide an effective, well-tolerated alternative or supplement to available therapies. In multi-center Phase I/II and Phase II trials, ALLOVECTIN-7 was well-tolerated, and provided durable reductions in overall tumor burden or maintained stable disease in some patients. Combined results from three Phase I/II trials, summarized in May 1998 at the Annual Meeting of the American Society of Clinical Oncology, included seven out of 36 evaluable patients, or 19 percent, who had achieved clinical partial or complete responses with a duration of at least eight months. We believe results from two Phase II melanoma trials indicated the potential efficacy of ALLOVECTIN-7 in treating melanoma patients, and suggested a negative correlation between disease spread and such potential efficacy. Among the 50 evaluable patients with widespread advanced disease affecting multiple internal organs, combined results from the two Phase II trials included:

- - two patients who had achieved a clinical response lasting two to 12 months and continuing at the time of the announcement, and

- - ten patients who had achieved stable disease lasting two to 11 months and continuing at the time of the announcement.

In patients with soft-tissue metastases in lymph nodes, lungs or tissues located directly beneath the skin, combined Phase II results included four of 23 evaluable patients, or 17 percent, who had achieved clinical partial responses with an average duration of 11 months. We believe the latter results compare favorably to available clinical data on other FDA-approved biological agents such as interferon-alpha and interleukin-2.

Updated data from the Phase I/II and Phase II trials, were presented in December 1999 at the Eighth International Gene Therapy of Cancer Conference. Of 90 evaluable end-stage patients, 24, or 26

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percent, demonstrated clinical benefit. Tumor regression was noted more often in patients with soft-tissue metastatic disease than in patients with multiple-internal organs affected. In the 32 patient soft-tissue subgroup, 12 patients, or 37 percent, demonstrated clinical benefit. The median time to disease progression was 24 weeks in patients who responded to ALLOVECTIN-7, compared with nine weeks in all patients. The median length of survival was 99 weeks for responders compared with 38 weeks in all patients.

Side effects from ALLOVECTIN-7 were primarily mild with the most common complaint being temporary pain at the injection site. No serious side effects related to ALLOVECTIN-7 were reported in these trials. This side-effect profile for ALLOVECTIN-7 compares favorably with available clinical data on other FDA-approved biological agents. Treatment with interferon-alpha or interleukin-2 frequently causes serious side effects requiring hospitalization, and occasionally causes life-threatening or fatal complications.

Based on this promising data, and following discussions with the FDA, we began registration trials in May 1998. These trials are ongoing in multiple centers across the United States. In our Phase II trial we are actively recruiting patients with soft-tissue metastatic melanoma who have exhausted conventional therapies. For our Phase III trial we are actively recruiting patients that have metastatic melanoma and who have not received chemotherapy. The objective of this trial is to compare treatment with dacarbazine, the only chemotherapeutic agent approved by the FDA for metastatic melanoma, to treatment with a combination of dacarbazine plus ALLOVECTIN-7. Positive results from either or both of these trials could allow us to apply to the FDA for approval to market ALLOVECTIN-7. We announced in December 1999 that we would continue to recruit patients as planned in our two ongoing registration trials with ALLOVECTIN-7 in patients with metastatic melanoma, based on the recommendations of an independent Drug Safety Review Board.

#### HEAD AND NECK CANCER

Head and neck cancer describes any of several types of localized tumors affecting the oral cavity, the pharynx or larynx. Head and neck cancers occur more frequently in men than in women, and most often in men over age 40. Risk factors vary with the particular location, but can include use of tobacco and excessive consumption of alcohol. The ACS estimates that, in 1999, 41,400 new cases of head and neck cancers will occur and that 12,300 individuals will die from this disease. NCI estimates that about 345,000 Americans currently suffer from head and neck cancer. Most head and neck cancers are treated by surgical removal and/or localized radiation therapy, with widely ranging degrees of success depending on the number of tumors, their size, and their specific location. In advanced disease, standard treatment may be preceded by systemic chemotherapy to improve outcomes, or followed by systemic chemotherapy to attack remaining cancer cells, most often with a combination of agents. The five-year survival rate for head and neck cancer patients, if treated, varies from more than 80 percent for localized, accessible disease to less than 20 percent for widespread malignancies not curable by surgery.

Treatment with ALLOVECTIN-7 in a Phase I/II and an early Phase II study yielded encouraging results, reported in May 1998 at the Annual Meeting of the American Society of Clinical Oncology, that included both partial and complete responses. Of the 11 patients treated in an investigator-sponsored Phase I/II clinical trial, four achieved complete or partial responses lasting at least five months. Preliminary results for 23 evaluable patients in a Vical-sponsored multi-center Phase II trial yielded one clinical complete response lasting four months and continuing, and 10 patients with stable disease after two to four months and continuing. A multi-center Phase II study is ongoing.

#### LEUVECTIN

LEUVECTIN is a DNA/lipid complex designed for direct injection into a tumor. LEUVECTIN contains the gene encoding IL-2. Systemic IL-2 protein

therapy is the only FDA-approved treatment for metastatic kidney disease, but its administration is associated with serious toxicity in the majority of patients. The LEUVECTIN kidney cancer program seeks to match IL-2's efficacy without major adverse events. We expect that LEUVECTIN, when injected into tumors, will cause the malignant cells to produce IL-2. Local expression of IL-2 may stimulate the patient's immune system to attack and destroy the tumor cells. Because LEUVECTIN delivers IL-2 locally rather than throughout the body, it may provide efficacy comparable to the protein treatment with fewer side effects. LEUVECTIN is being tested in Phase II clinical trials for patients with kidney cancer and prostate cancer.

#### KIDNEY CANCER

The most common type of kidney cancer, renal cell carcinoma, occurs more frequently in males than in females, and predominantly in people over 35. The greatest single risk factor is cigarette smoking. Other risk factors include exposure to asbestos, cadmium, or gasoline, and the use of some former pain medications containing phenacetin. According to ACS statistics, 29,900 new cases of kidney cancer will be diagnosed in the U.S. and 11,600 patients will die from the disease in 1999. NCI estimates that about 200,000 Americans currently suffer from kidney cancer. Primary kidney cancer frequently spreads to adjacent tissues and ultimately to other internal organs, most often the lungs, bone, brain or liver. About 30 percent of patients have metastatic disease when first diagnosed. Treatment of regional metastatic kidney cancer involves surgical removal of the affected kidney and surrounding tissue, and frequently is combined with radiation therapy to alleviate pain.

There are few treatment alternatives for metastatic kidney cancer and where surgery cannot be curative the five year survival rate is less than 10 percent. Initial results from Phase I/II and Phase II testing in kidney cancer indicated that LEUVECTIN was well-tolerated and effective in delivering the IL-2 protein, with a favorable risk-benefit profile in these patients. A multi-center Phase II study initiated in May 1998 is ongoing. Initial results from the Phase II trial were reported in May 1999 at the Annual Meeting of the American Society of Clinical Oncology. Four of the 22 evaluable patients, or 18 percent, experienced significant tumor reductions of 25 percent or more, including one patient who experienced 90 percent and 100 percent reductions in two non-injected tumors. Twelve additional patients, or 55 percent, had stabilization of the injected tumor for six to 28 weeks and continuing at the time of the meeting. Six of the 22 patients, or 27 percent, experienced clinical stable disease for five to seven months and continuing at the time of the meeting. Side effects from the LEUVECTIN treatment were primarily mild, with the most common complaint being flu-like symptoms of chills, low-grade fever, body aches and fatigue. The only serious side effects reported were two incidents of severe pain at the injection site. Both were resolved with pain medication during brief hospital stays.

#### PROSTATE CANCER

Prostate cancer is the most frequently diagnosed type of cancer and is the second leading cause of cancer fatalities among men in the United States. Men over age 65 account for over 75 percent of all diagnoses and African Americans are at significantly greater risk than Caucasians. According to ACS statistics, 179,300 new cases of prostate cancer will be diagnosed in the U.S. and 37,000 patients will die from this disease in 1999. NCI estimates that more than one million American men currently suffer from prostate cancer. Early detection is increasing the number of annual diagnoses and improving overall survival rates. All patients diagnosed while the disease is confined to the prostate gland have a five-year survival rate. If the disease is discovered after it spreads to connective tissue, lymph nodes, or other internal organs, survival rates decline. Treatment options include "watchful waiting" for older patients with no symptoms or with other more serious illnesses, radiation therapy or cryosurgery, and surgical removal of the prostate gland and/or affected lymph nodes. Symptoms may also be relieved by hormone therapy or surgery.

A Phase I/II pilot trial tested LEUVECTIN in patients with prostate cancer. The data indicated that the treatment was safe and well-tolerated, that it may stimulate an immune response against the disease, and that it may result in an increased time to disease progression. Results of the trial were presented in May 1999 at the Annual Meeting of the American Urological Association. In eight of 12 patients scheduled for surgery, pre-surgical serum PSA levels decreased significantly after treatment with LEUVECTIN. Three patients were diagnosed with metastatic disease at the time of the surgery and were therefore excluded from the trial. All nine patients who remained in the trial after surgery maintained negligible PSA levels after 11 to 18 months and continuing at the time of the meeting. In seven of nine patients with progressive disease following radiation therapy, serum PSA levels decreased significantly after treatment with LEUVECTIN. In four of five patients receiving a second treatment course of LEUVECTIN, the rate of increase in PSA levels was reduced considerably. On the basis of these data,



#### CANCER VACCINES

In collaboration with Stanford University Medical Center, we are developing a naked DNA vaccine, Vaxid, against low-grade, non-Hodgkin's, B-cell lymphoma. Non-Hodgkin's B-cell lymphoma is a disease in which cells in the lymph nodes or other lymphatic tissue grow abnormally. Low-grade non-Hodgkin's B-cell lymphoma exhibits a slow growth rate and excellent initial response to current treatments. However, a regular pattern of relapse to a widespread, aggressive lymphoma occurs for which no curative therapy has been identified. According to ACS statistics, 56,800 new cases of B-cell lymphoma will be diagnosed in the U.S. and 25,700 patients will die from this disease in 1999. NCI estimates that about 300,000 Americans currently suffer from B-cell lymphoma.

VAXID contains a patient-specific gene encoding a characteristic molecule of cancerous B-cells. Preclinical studies showed that the injection into mice of a DNA vaccine that encoded a gene specific to the B-cell lymphoma resulted in strong and specific immune responses and significant protection against subsequent tumor challenge. We believe that immunization of post-chemotherapy patients with VAXID could result in the elimination of residual disease and the prevention of the relapse of disease. An initial Phase I/II study of VAXID is ongoing.

In collaboration with the NCI we are supporting the development of another DNA vaccine which may cause cells to produce a modified melanoma-related protein known as gp100. This protein is expected to trigger an immune response against melanoma tumor cells. In earlier studies, the NCI tested a vaccine using portions of the modified protein in combination with IL-2 protein therapy. These data indicated a 42 percent response rate in end-stage melanoma patients after treatment with systemic IL-2 and the gp100 protein. This study is being repeated with a gp100 naked DNA vaccine provided by us. We believe a DNA vaccine may be more generally applicable and may provide advantages in manufacturing and administration.

#### DNA VACCINES FOR INFECTIOUS DISEASES

According to the World Health Organization, infectious and parasitic diseases cause approximately one-third of all deaths worldwide, making it the leading cause of death. Most deaths from infectious diseases are caused by acute lower respiratory infections, tuberculosis, neonatal diarrhea, AIDS and malaria. Vaccines are generally recognized as the most cost-effective approach for infectious disease health care. However, the technical limitations of conventional vaccine approaches have constrained the development of effective vaccines for many diseases.

Our naked DNA vaccine technology may overcome two deficiencies of traditional preventive vaccine approaches, which are the inability to counteract the random changes in the strains of various infectious agents and the need for safe formulations that boost an antibody response or that cause sufficient killer T-cell responses, known as adjuvants. We believe our potential vaccine products should be simpler to manufacture than vaccines that are made using cumbersome and labor-intensive techniques involving difficult tissue culture procedures and live viruses.

Our scientists have shown in animal experiments that the intramuscular injection of plasmid DNA encoding a protein common to all strains of the influenza virus stimulates both antibody and killer T-cell responses against the virus itself and virus-infected cells. The immune response is potent, specific and requires no adjuvants. For over a year following vaccination, treated animals demonstrated higher survival rates than untreated control animals when challenged with various strains of inhaled influenza virus. This observed cross-strain protection, if reproducible in humans, will offer a key advantage compared with conventional vaccines. Thus, our direct gene delivery technology may be universal, not requiring frequent re-design or product modification for each new viral strain.

Only a few years ago, DNA vaccines were an unproven novelty with limited acceptance in the scientific community. Today, numerous scientific publications have documented the efficacy of DNA vaccines in providing potent immune responses or protective immunity against viruses, bacteria and parasites in dozens of species from fish to primates, including human volunteers. Additional studies have extended these findings to other models of infectious diseases for which there are no approved vaccines, such as HIV, herpes and malaria.

capacity and distribution channels required to successfully market a vaccine, we believe collaborations with major pharmaceutical companies are the most effective way to apply our patented technology in the emerging DNA vaccine field. We have long-standing, active partnerships with two of the three largest vaccine manufacturers in the world, Merck and Aventis Pasteur. These relationships are summarized below. Further details can be found in "--Collaboration and Licensing Agreements--Corporate Partners."

#### MERCK

We have licensed our naked DNA vaccination technology to Merck for a total of seven preventive vaccine targets:

- - hepatitis B virus, HBV,
- - hepatitis C virus, HCV,
- - human immunodeficiency virus, HIV,
  - human papilloma virus, HPV,
  - herpes simplex virus, HSV,
  - influenza virus, and
  - tuberculosis, TB.

In addition, Merck also has a license covering three therapeutic vaccine targets, HBV, HIV and HPV.

In December 1999, Merck initiated a clinical trial with a naked DNA vaccine to prevent AIDS. In January 2000, we received \$1.0 million from Merck following initiation of this clinical trial. This candidate vaccine product is being developed by Merck under the license agreement with us. In November 1999, we received a \$2.0 million payment from Merck which extends Merck's exclusive license to develop and market therapeutic vaccines against HIV and HBV.

#### AVENTIS PASTEUR, FORMERLY PASTEUR MERIEUX CONNAUGHT

We also have a license and option agreement with Aventis Pasteur, formerly Pasteur Merieux Connaught, for a total of six preventive vaccine targets:

- - cytomegalovirus, CMV,
- - HELICOBACTER PYLORI,
- - Lyme disease,
- - malaria,
- - respiratory syncytial virus, RSV, and
- - varicella zoster virus, VZV.

We are collaborating with Aventis Pasteur and the U.S. Naval Medical Research Center, NMRC, to develop a DNA vaccine against malaria. There is no effective vaccine against malaria. This is a severe infectious disease characterized by fever, headache and joint pain, which if untreated can lead to death. Infection normally occurs when the parasite enters a victim's bloodstream during a mosquito bite. Each year, 300 to 500 million people worldwide are treated for malaria and more than one million die from the disease, according to the World Health Organization.

In July 1997, in collaboration with Aventis Pasteur, we began a Phase I trial of an experimental vaccine against the parasite that causes malaria. NMRC conducted the clinical trial with approximately twenty volunteers. Trial results, reported in the October 16, 1998, issue of SCIENCE, indicated that subjects immunized with a potential malaria DNA vaccine developed dose-related killer T-cell immune responses. As a result of these encouraging data, further clinical development is planned.

#### DNA THERAPEUTIC PROTEIN DELIVERY

Our naked DNA direct gene delivery technology also may permit the development of alternatives to therapeutic protein administration for diseases. Major shortcomings of some therapeutic proteins include their short duration of action and the potential side effects associated with high levels of circulating protein after intravenous administration. We believe that direct injection into muscles of genes that encode the protein of interest may enable the muscle cells to act as protein factories causing a sustained release of low levels of the therapeutic proteins, reducing side effects and the need for repeated dosing. Our technology may be most suitable for the delivery of proteins that are required in small amounts over prolonged periods of time.

Much attention is being focused on the emerging field of angiogenesis, which involves inducing the growth of new blood vessels to replace those blocked by disease. DNA-based delivery of growth factors has been successfully demonstrated in human trials. Other potential applications, still being tested in animal models, could involve the delivery of proteins that maintain nerve cell function for treating certain neurodegenerative diseases, or the delivery of biologically active compounds such as insulin to

treat diabetes or erythropoietin to treat certain forms of anemia.

In 1998, we licensed our catheter-based intravascular gene delivery technology, with potential angiogenesis applications, to Boston Scientific.

On February 24, 2000, the Company and Human Genome Sciences, Inc. (HGS) signed a reciprocal royalty-bearing license. Under the agreement, Vical has the option to exclusively license up to three genes from HGS for gene-based product development. HGS has the option to license Vical's naked DNA gene delivery technology for use in up to three gene-based products. Vical also granted an exclusive, royalty-bearing license to Vascular Genetics Inc., VGI, for naked DNA delivery of Vascular Endothelial Growth Factor-2 (VEGF-2). VGI, a privately held company in which HGS is a major shareholder, has initiated clinical trials using naked DNA delivery of the VEGF-2 gene to promote angiogenesis in patients with coronary artery disease and critical limb ischemia.

We licensed our naked DNA gene delivery technology to Rhone-Poulenc Rorer, now Aventis Pharma, in 1997 for the delivery of neurologically active proteins that may be applicable in treating neurodegenerative diseases such as Alzheimer's, Parkinson's and Lou Gehrig's diseases.

#### VETERINARY APPLICATIONS

Prior to its development for human therapy, our naked DNA gene delivery technology was extensively tested in animals. Research scientists have published numerous papers detailing favorable results in many species and covering a broad range of disease indications. Animal health encompasses two distinct market segments: livestock, or animals bred and raised for food or other products; and companion animals, or pets. Serving the animal health markets requires highly efficient manufacturing and specialized distribution channels. Consequently, we have licensed our naked DNA technology to leading animal health pharmaceutical companies for development and commercialization.

#### DNA VACCINES FOR VETERINARY INFECTIOUS DISEASES

We entered into a corporate alliance in March 1995 relating to DNA vaccines in the animal health area with Merial, a joint venture between Merck and Rhone Merieux. Merial has options to acquire exclusive licenses to our gene delivery technologies to develop and commercialize DNA-based vaccines to prevent infectious diseases in domesticated animals. Through September 30, 1999, we had received \$3.2 million under this agreement. In December 1999, Merial paid us \$1.6 million for the initial exercise of options under the agreement. If Merial exercises additional license options and markets these vaccines, cash payments and royalties on sales would be due to us.

#### VETERINARY DNA THERAPEUTIC PROTEIN DELIVERY

In January 1999, we entered into a collaborative research, license, and option agreement granting Pfizer rights to use our patented naked DNA gene delivery technologies to deliver certain therapeutic proteins for animal health applications. Pfizer made an initial investment of \$6.0 million in our common stock, paid an initial fee of \$1.0 million, and agreed to fund our research totaling \$1.5 million for the first three years of the collaboration. We may receive milestone payments and royalties if products are

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successfully developed under the agreement. In addition, we may manufacture products resulting from the collaboration for Pfizer.

#### INTELLECTUAL PROPERTY

Patents and other proprietary rights are essential to our business. We file patent applications to protect our technology, inventions, and improvements to our inventions that we consider important to the development of our business.

We also rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. We have filed or participated as licensee in the filing of more than 35 patent applications in the United States and have made over 280 additional counterpart foreign filings in foreign countries relating to our technology. Our patent applications seek to cover naked DNA gene delivery for immunization and to deliver therapeutic proteins to patients, specific gene sequences and formulations of gene-based product candidates, methods for producing pharmaceutical-grade DNA and the composition of matter of several families of lipid molecules and their uses in gene delivery. Many of these patents have been issued by the U.S. Patent and Trademark Office. Several other applications are still pending in the United States, and corresponding foreign applications have been filed.

We and our exclusive licensors have received numerous U.S. and

foreign patents covering various aspects of our proprietary technology. Most of these patents are recently issued and have considerable patent life remaining. These patents are described as follows:

- - CORE DNA DELIVERY TECHNOLOGY. We have received issued U.S. patents covering our core DNA therapeutics technology, including patents on methods of administering gene sequences for the purposes of expressing therapeutic proteins or for inducing immune responses. Other issued patents specifically cover the administration of genes into blood vessels and the heart. Patent coverage of our core DNA delivery technology has also been obtained in Europe.
- - CORE LIPID TECHNOLOGY. We have received issued U.S. patents covering numerous examples of cationic lipid compounds that are used to facilitate delivery of DNA therapeutics to some tissues. These patented compounds include the lipids contained in our lead product candidates, ALLOVECTIN-7 and Leuvectin. Patent protection of these key lipids also has been obtained in Europe and Japan.
- - SPECIFIC DNA THERAPEUTICS. We have supplemented the broad patent coverage described above with patents covering specific product applications of our technology. To date, we have received patents issued in the U.S. covering the DNA components of ALLOVECTIN-7 and Leuvectin.
- - DNA PROCESS TECHNOLOGY. As a result of our pioneering efforts to develop the use of pure DNA as a therapeutic agent, we have also led the development of manufacturing processes for producing pharmaceutical-grade DNA. We have received issued U.S. patents covering various steps involved in the process of economically producing pure plasmid DNA for pharmaceutical use.

Two of our allowed U.S. patent applications have been suspended from issuance by the United States Patent & Trademark Office pending possible interference proceedings with one or more parties unknown to us. The suspension may be lifted or the application(s) may be drawn into interference. According to European patent procedures, issued patents may be opposed by parties interested in challenging the scope or validity of the issued claims. A European patent covering our core DNA delivery technology is currently being opposed by several companies under these procedures. We intend to vigorously defend our patent position in these opposition proceedings. An unfavorable result in these opposition proceedings could cause us to lose part or all of our proprietary protection on our potential products in Europe. We believe that no others hold patents or other intellectual property that would preclude us from commercializing our proprietary technology.

Some components of our gene-based product candidates are, or may become, patented by others. As a result, we may be required to obtain licenses to conduct research, to manufacture or to market such products. Licenses may not be available on commercially reasonable terms, or at all.

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See "--Risk Factors--Our Patents and Proprietary Rights May Not Provide Us With Any Benefit and the Patents of Others May Prevent Us From Commercializing Our Products" and "The Legal Proceedings to Obtain Patents and Litigation of Third-Party Claims of Intellectual Property Infringement Could Require Us to Spend Money and Could Impair Our Operations."

#### COMMERCIALIZATION AND MANUFACTURING

Because of the broad potential applications of our technology, we intend to develop and commercialize products both on our own and through corporate partners. We intend to develop and market products to well-defined specialty markets, such as oncology, infectious diseases and other life-threatening diseases. Where appropriate, we intend to rely on strategic marketing and distribution partners for manufacturing and marketing products.

We believe our DNA plasmids can be produced in commercial quantities through conventional fermentation and purification techniques. The separation and purification of plasmid DNA is a relatively straightforward procedure because of the inherent biochemical differences between plasmid DNA and the majority of other bacterial components. In addition, our lipid formulations consist of components that are synthesized chemically using traditional, readily scaleable, organic synthesis procedures.

We produce and supply our product for all of our clinical trials and intend to produce sufficient supplies for additional clinical investigations. We may also choose to have outside organizations manufacture our product candidates for expanded clinical trials under close supervision utilizing our proprietary processes.

#### COLLABORATION AND LICENSING AGREEMENTS

We have entered into various arrangements with corporate, academic and government collaborators, licensors, licensees and others. In addition to the agreements summarized below, we conduct ongoing negotiations with

potential corporate partners.

#### CORPORATE PARTNERS

MERCK & CO., INC. In May 1991, we entered into a research collaboration and license agreement with Merck to develop vaccines utilizing our intramuscular delivery technology to prevent infection and disease in humans. In connection with the 1991 agreement, we granted Merck a worldwide exclusive license to preventive vaccines using our technology against seven human infectious diseases including influenza, HIV, herpes simplex, HBV, HCV, HPV and tuberculosis. Merck has the right to terminate this agreement without cause on 90 days written notice.

In addition, Merck has rights to therapeutic uses of preventive vaccines developed under the 1991 agreement. In December 1995 and November 1997, Merck acquired additional rights to develop and market therapeutic vaccines against HPV, HIV and HBV. Under the November 1997 amendment, Merck made an investment of \$5.0 million for approximately 262,000 shares of our common stock.

In September 1997, we entered into an option and license agreement granting Merck the rights to use our technology to deliver certain growth factors. The agreement resulted in a payment to us of \$2.0 million. In March 2000, Merck notified us of its intent to terminate this agreement effective June 2000.

In connection with these agreements, Merck has paid us \$21.1 million as of December 31, 1999. In November 1999, we received a \$2.0 million payment from Merck which extends Merck's exclusive license to develop and market therapeutic vaccines against HIV and HBV. In December 1999, Merck initiated a clinical trial with a naked DNA vaccine to prevent AIDS. In January 2000, Merck paid us a \$1.0 milestone payment for the start of this trial. Merck is obligated to pay additional fees if research milestones are achieved and royalties on net sales if any products are developed and marketed. For some indications we may have an opportunity to co-promote product sales.

AVENTIS PASTEUR, FORMERLY PASTEUR MERIEUX CONNAUGHT. In September 1994, we entered into a research, option and license agreement with the vaccine manufacturer Pasteur Merieux Connaught, now Aventis Pasteur, granting Aventis Pasteur options to acquire licenses for the use of our proprietary DNA delivery and technologies for developing vaccines against CMV, RSV, Lyme disease, HELICOBACTER PYLORI

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and malaria. In April 1996, varicella zoster was added. Aventis Pasteur has exercised its option to acquire several of these licenses. Aventis Pasteur is obligated to make milestone and royalty payments to us if any products are developed and marketed. In July 1997, Aventis Pasteur paid us \$1.0 million as a milestone payment upon initiation of a Phase I trial of an experimental vaccine against the parasite that causes malaria. Through December 31, 1999, we had received \$7.8 million under this agreement.

PFIZER INC. In January 1999, we entered into a collaborative research and option agreement with Pfizer to develop and market DNA-based delivery of therapeutic proteins for animal health applications. Pfizer has an option to obtain an exclusive royalty-bearing license to our technology for these applications. The option expires in January 2002. Under the agreement, Pfizer made an investment of \$6.0 million for approximately 318,000 shares of our common stock. Pfizer also paid us a \$1.0 million up-front license fee, and is obligated to pay us \$1.5 million for research and development over the first three years of the agreement. Through December 31, 1999, Pfizer had paid us \$0.5 million of this \$1.5 million obligation.

MERIAL. We entered into a corporate alliance in March 1995 relating to DNA vaccines in the animal health area with Merial, a joint venture between Merck and Rhone Merieux. Merial has options to take exclusive licenses to our DNA delivery technologies to develop and commercialize DNA-based vaccines to prevent infectious diseases in domesticated animals. In December 1999, Merial paid us \$1.6 million for the initial exercise of options and extension of options under the agreement. Through December 31, 1999, we had received \$4.8 million under this agreement. If Merial exercises additional license options and markets these vaccines, cash payments and royalties on sales would be due to us. Merial has the right to terminate this agreement without cause on 30 days written notice.

HUMAN GENOME SCIENCES, INC. AND VASCULAR GENETICS INC. On February 24, 2000, the Company and Human Genome Sciences, Inc. (HGS) signed a reciprocal royalty-bearing license. Under the agreement, Vical has the option to exclusively license up to three genes from HGS for gene-based product development. HGS has the option to license Vical's naked DNA gene delivery technology for use in up to three gene-based products. In addition, the Company granted an exclusive, royalty-bearing license to Vascular Genetics Inc. (VGI), a company in which HGS is a major shareholder, for naked DNA delivery of a gene with potential use for revascularization. In exchange,

Vical received a minority equity interest in VGI.

AVENTIS PHARMA, FORMERLY RHONE-POULENC RORER PHARMACEUTICALS, INC. In October 1997, we entered into an agreement with Rhone-Poulenc Rorer Pharmaceuticals, Inc., now Aventis Pharma, granting Aventis Pharma an exclusive worldwide license to use our naked DNA delivery technology to deliver certain neurologically active proteins for potential treatment of neurodegenerative diseases. Under the terms of the agreement, we received \$1.0 million in 1997. This agreement provides for us to receive additional payments based upon achievement of milestones and royalty payments on product sales.

CENTOCOR, INC. In February 1998, we entered into an exclusive license and option agreement allowing Centocor, Inc., subsequently acquired by Johnson & Johnson, to use our naked DNA technology to develop and market certain DNA-based vaccines for the potential treatment of some types of cancer. We received an initial payment of \$2.0 million plus reimbursement of \$0.2 million of patent costs. We may receive additional payments based upon achievement of milestones and royalty payments on product sales.

BOSTON SCIENTIFIC CORPORATION. In April 1997, we entered into a sublicense agreement with Cardiogene Therapeutics, Inc., formerly known as Genocor, Inc., for the development of catheter-based intravascular gene delivery technology under our license agreement with the University of Michigan described below. Boston Scientific Corporation has subsequently acquired Cardiogene Therapeutics' rights under this agreement. We received \$1.1 million in October 1998 under this agreement. The agreement provides for us to receive royalty payments on any related product sales.

Under the Merck, Aventis Pasteur, Merial, Aventis Pharma, Centocor, Pfizer, Human Genome Sciences, Inc. and Vascular Genetics Inc. agreements, if we were to receive milestone or royalty payments, we would be required to pay up to 10 percent of some of these payments to Wisconsin Alumni Research Foundation. Under the Boston Scientific agreement, if we were to receive milestone or royalty payments, we would be required to pay up to 25 percent of some of these payments to the University of

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Michigan. See "--Research Institutions--Wisconsin Alumni Research Foundation" and "--Research Institutions--The University of Michigan."

#### RESEARCH INSTITUTIONS

OFFICE OF NAVAL RESEARCH. In September 1998, we entered into an agreement with the Office of Naval Research, ONR, for the development work on a potential multi-gene DNA vaccine to prevent malaria. This agreement could provide total funding of up to \$2.8 million through 2000, of which \$2.3 million was recognized as revenue through December 31, 1999. We intend to pursue additional agreements with ONR to continue funding for this development program, however, we may not be able to enter into any further agreements.

THE UNIVERSITY OF MICHIGAN. In October 1992, we entered into a license agreement with the University of Michigan and obtained the exclusive license to technology for delivering gene-based products into cancer cells and blood vessels by catheters. In April 1997, we entered into a sublicense agreement, the rights under which are currently held by Boston Scientific Corporation, for the development of catheter-based intravascular gene delivery technology.

WISCONSIN ALUMNI RESEARCH FOUNDATION, WARF. Under a 1989 research agreement, scientists at the University of Wisconsin, Madison, and our scientists co-invented a core technology related to intramuscular naked DNA administration. In 1991, we licensed from WARF its interest in that technology. We paid WARF an initial license fee and agreed to pay WARF a royalty on sales of any products incorporating the licensed technology and a percentage of up-front license payments from third parties.

#### COMPETITION

The field of gene-based drug development is new and rapidly evolving, and it is expected to continue to undergo significant and rapid technological change. Rapid technological development could result in our potential products or technologies becoming obsolete before we recover a significant portion of our related research, development and capital expenditures. We may experience competition both from other companies in the field and from companies which have other forms of treatment for the diseases we are targeting.

We are aware of several development-stage and established enterprises, including major pharmaceutical and biotechnology firms, which are exploring gene-based drugs or are actively engaged in gene delivery research and development. These include Avigen, Targeted Genetics Corp., Transgene SA and Valentis Inc. We may also experience competition from

companies that have acquired or may acquire technology from companies, universities and other research institutions. As these companies develop their technologies, they may develop proprietary positions which may materially and adversely affect us.

In addition, a number of companies are developing products to address the same disease indications that we are targeting. For example, Maxim Pharmaceuticals, Inc. and Corixa Corp. are conducting advanced clinical trials for the treatment of melanoma. As another example, Aventis, Onyx Pharmaceuticals, Inc. and ImClone Systems Incorporated are conducting clinical trials of their products to treat head and neck cancer. If these or any other companies develop products with efficacy or safety profiles significantly better than our products, we may not be able to commercialize our products and sales of any of our commercialized products could be harmed.

Some competitors and potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than we do. Other companies may develop products earlier, obtain FDA approvals for products more rapidly, or develop products that are more effective than those under development by us. We will seek to expand our technological capabilities to remain competitive; however, research and development by others may render our technology or products obsolete or noncompetitive or result in treatments or cures superior to ours.

Our competitive position will be affected by the disease indications addressed by our potential products and those of our competitors, the timing of market introduction for these potential products and the stage of development of other technologies to address these disease indications. For us and our competitors, proprietary positions, the ability to complete clinical trials on a timely basis and with the desired results, and the ability to obtain timely regulatory approvals to market these potential products are

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likely to be significant competitive factors. Other important competitive factors will include the efficacy, safety, reliability, availability and price of potential products and the ability to fund operations during the period between technological conception and commercial sales.

#### GOVERNMENT REGULATION

Any products we develop will require regulatory clearances prior to clinical trials and additional regulatory clearances prior to commercialization. New human DNA therapeutics are expected to be subject to extensive regulation by the FDA and comparable agencies in other countries. The precise regulatory requirements with which we will have to comply are uncertain at this time due to the novelty of the DNA-based products and therapies currently under development. We believe that our potential products will be regulated either as biological products or as drugs. Drugs are subject to regulation under the Federal Food, Drug and Cosmetic Act, and biological products, in addition to being subject to provisions of that Act, are regulated under the Public Health Service Act. Both statutes and related regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, storage, record keeping, advertising and other promotional practices. FDA approval or other clearances must be obtained before clinical testing, and before manufacturing and marketing of biologics or drugs.

FDA approval is required prior to marketing a pharmaceutical product in the United States. To obtain this approval the FDA requires clinical trials to demonstrate the safety, efficacy, and potency of the product candidates. Clinical trials are the means by which experimental drugs or treatments are tested in humans. New therapies typically advance from laboratory, research, testing through animal, preclinical, testing and finally through several phases of clinical, human, testing. Upon successful completion of clinical trials, approval to market the therapy for a particular patient population may be requested from the FDA in the United States and/or its counterparts in other countries.

Clinical trials are normally done in three phases. In Phase I, trials are conducted with a small number of patients or healthy volunteers to determine the safety profile, the pattern of drug distribution and metabolism and early evidence on effectiveness. In Phase II, trials are conducted with a larger group of patients afflicted with a target disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety. In Phase III, large scale, multi-center, comparative trials are conducted with patients afflicted with a target disease in order to provide enough data for the statistical proof of safety, efficacy, and potency required by the FDA and other regulatory authorities. For life-threatening diseases, initial human testing generally is done in patients rather than healthy volunteers. These studies may provide results traditionally obtained in Phase II trials and are referred to as "Phase I/II" trials.

Obtaining FDA approval has been a costly and time-consuming process.

Generally, in order to gain FDA pre-market approval, preclinical studies must be conducted in the laboratory and in animal model systems to gain preliminary information on an agent's efficacy and to identify any major safety concerns. The results of these studies are submitted as a part of an application for an Investigational New Drug, IND, which the FDA must review and allow before human clinical trials can start. The IND includes a detailed description of the clinical investigations.

A company must sponsor and file an IND for each proposed product and must conduct clinical studies to demonstrate the safety, efficacy and potency that are necessary to obtain FDA approval. The FDA receives reports on the progress of each phase of clinical testing, and it may require the modification, suspension, or termination of clinical trials if an unwarranted risk is presented to patients. Human DNA therapeutics are a new category of therapeutics, and the clinical trial period may be lengthy or the number of patients may be numerous in order to establish safety, efficacy and potency.

After completion of clinical trials of a new product, FDA marketing approval must be obtained. If the product is regulated as a biologic, a Biologic License Application, BLA, is required. If the product is classified as a new drug, a New Drug Application, NDA, is required. The NDA or BLA must include results of product development activities, preclinical studies and clinical trials in addition to detailed manufacturing information.

Applications submitted to the FDA are subject to an unpredictable and potentially prolonged approval process. The FDA may ultimately decide that the application does not satisfy its criteria for approval or require additional preclinical or clinical studies. Even if FDA regulatory clearances are

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obtained, a marketed product is subject to continual review, and later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Before marketing clearance is secured, the manufacturing facility will be inspected for current Good Manufacturing Practices, GMP, compliance by FDA inspectors. The manufacturing facility must satisfy current GMP requirements prior to marketing clearance. In addition, after marketing clearance is secured, the manufacturing facility will be inspected periodically for GMP compliance by FDA inspectors, and, if the facility is located in California, by inspectors from the Food and Drug Branch of the California Department of Health Services.

In addition to the FDA requirements, the NIH has established guidelines for research involving recombinant DNA molecules. These guidelines apply to all recombinant DNA research which is conducted at or supported by the NIH, including proposals to conduct clinical research involving DNA therapeutics. The NIH review of clinical trial proposals is a public process and usually involves review and approval by the Recombinant DNA Advisory Committee of the NIH.

In both domestic and foreign markets, sales of any approved products will depend on reimbursement 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. If we succeed in bringing one or more products to market, these products may not be considered cost-effective, reimbursement may not be available, or reimbursement policies may adversely affect our ability to sell our products on a profitable basis.

We also are subject to various federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research. The extent of government regulation which might result from any future legislation or administrative action cannot be accurately predicted.

#### HUMAN RESOURCES

As of March 1, 2000, we had 119 full-time employees, 22 of whom hold degrees at the doctorate level. Of these employees, 89 are engaged in, or directly support, research and development activities, and 30 are in administrative and business development positions. A significant number of our management and professional employees have prior experience with pharmaceutical and biotechnology companies. None of our employees is covered by collective bargaining agreements, and our management considers relations with our employees to be good.

#### FACILITIES

We lease approximately 43,000 square feet of manufacturing, research



laboratory and office space in an established commercial neighborhood in northern San Diego, California at three sites and with three leases. The leases terminate in 2004. We have the option to renew two of these three leases for an additional five-year period and can renew one of the leases for two additional five-year periods.

Within our existing facilities, we have manufactured sufficient quantities of pharmaceutical-grade product to supply our previous and ongoing clinical trials, including the current registration trials. In addition, we have manufactured preclinical and clinical supplies of DNA for our corporate partners, for government agencies and for numerous academic researchers. We believe that the build-out of unfinished space in our facilities will be sufficient to accommodate manufacturing of initial production quantities of our most advanced product candidates.

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#### RISK FACTORS

YOU SHOULD CAREFULLY CONSIDER THE RISKS DESCRIBED BELOW, TOGETHER WITH ALL OF THE OTHER INFORMATION INCLUDED IN THIS REPORT, BEFORE DECIDING WHETHER TO INVEST IN OUR COMMON STOCK. IF ANY OF THE FOLLOWING RISKS ACTUALLY OCCURS, OUR BUSINESS, FINANCIAL CONDITION OR RESULTS OF OPERATIONS COULD BE HARMED. IN THIS CASE, THE TRADING PRICE OF OUR COMMON STOCK COULD DECLINE, AND YOU MAY LOSE ALL OR PART OF YOUR INVESTMENT.

NONE OF OUR PRODUCTS HAVE BEEN APPROVED FOR SALE. IF WE DO NOT DEVELOP COMMERCIALY SUCCESSFUL PRODUCTS, WE MAY BE FORCED TO CURTAIL OR CEASE OPERATIONS.

Very little data exists regarding the safety and efficacy of DNA therapeutics. All of our potential products are either in research or development. We must conduct a substantial amount of additional research and development before any U.S. or foreign regulatory authority will approve any of our products. Results of our research and development activities may indicate that our potential products are unsafe or ineffective. In this case, regulatory authorities will not approve them. Even if approved, our products may not be commercially successful. If we fail to develop and commercialize our products, we will not be successful.

WE HAVE A HISTORY OF NET LOSSES. WE EXPECT TO CONTINUE TO INCUR NET LOSSES AND WE MAY NOT ACHIEVE OR MAINTAIN PROFITABILITY.

We have not sold any products and do not expect to sell any products for the next few years. For the period from our inception to December 31, 1999, we have incurred cumulative net losses totaling approximately \$44.6 million. Moreover, our negative cash flow and losses from operations will continue and increase for the foreseeable future. We may never generate sufficient product revenue to become profitable. We also expect to have quarter-to-quarter fluctuations in revenues, expenses and losses, some of which could be significant.

WE MAY NEED ADDITIONAL CAPITAL IN THE FUTURE. IF ADDITIONAL CAPITAL IS NOT AVAILABLE, WE MAY HAVE TO CURTAIL OR CEASE OPERATIONS.

We may need to raise more money to continue the research and development necessary to bring our products to market and to establish manufacturing and marketing capabilities. We may seek additional funds through public and private stock offerings, arrangements with corporate partners, borrowings under lease lines of credit or other sources. In the event that we need more money, but are unable to raise more money we may have to reduce our capital expenditures, scale back our development of new products, reduce our workforce and license to others products or technologies that we otherwise would seek to commercialize ourselves. The amount of money we may need will depend on many factors, including:

- the progress of our research and development programs,
- the scope and results of our preclinical studies and clinical trials,
- the time and costs involved in:
  - obtaining necessary regulatory approvals,
  - filing, prosecuting and enforcing patent claims,
  - scaling up our manufacturing capabilities, and
- the commercial arrangements we may establish.

THE REGULATORY APPROVAL PROCESS IS EXPENSIVE, TIME CONSUMING AND UNCERTAIN WHICH MAY PREVENT US FROM OBTAINING REQUIRED APPROVALS FOR THE COMMERCIALIZATION OF OUR PRODUCTS.

Testing of the potential drugs we develop is regulated by numerous governmental authorities in the United States and other countries. The regulations are evolving and uncertain. The regulatory process can take many years and require us to expend substantial resources. For example:

- - the U.S. Food and Drug Administration, the FDA, has not established guidelines concerning the scope of clinical trials required for DNA

- - the FDA has not indicated how many patients it will require to be enrolled in clinical trials to establish the safety and efficacy of DNA therapeutics, and
- - current regulations are subject to substantial review by various governmental agencies.

Therefore, U.S. or foreign regulations could prevent or delay regulatory approval of our products or limit our ability to develop and commercialize our products. Delays could:

- - impose costly procedures on our activities,
- - diminish any competitive advantages that we attain, and
- - negatively affect our ability to receive royalties.

We believe that the FDA and comparable foreign regulatory bodies will regulate separately each product containing a particular gene depending on its intended use. Presently, to commercialize any product we must sponsor and file a regulatory application for each proposed use. We then must conduct clinical studies to demonstrate the safety and efficacy of the product necessary to obtain FDA approval. The results obtained so far in our clinical trials may not be replicated in our on-going or future trials. This may prevent any of our potential products from receiving FDA approval.

We use recombinant DNA molecules in our product candidates, and therefore we also must comply with guidelines instituted by the National Institutes of Health, the NIH, and its Recombinant DNA Advisory Committee. The NIH could restrict or delay the development of our products.

ADVERSE EVENTS IN THE FIELD OF GENE THERAPY, OR WITH RESPECT TO OUR POTENTIAL PRODUCTS, MAY NEGATIVELY IMPACT REGULATORY APPROVAL OR PUBLIC PERCEPTION OF OUR PRODUCTS.

The recent death of a patient undergoing a viral-based gene therapy at the University of Pennsylvania in an investigator sponsored trial has been widely publicized. This death and other adverse events in the field of gene therapy could result in greater governmental regulation of gene therapies, including our non-viral naked DNA technology, and potential regulatory delays relating to the testing or approval of our potential products. In addition, the field of gene therapy is under increased scrutiny, which may affect our product development efforts or clinical trials.

For example, one patient who had undergone treatment with ALLOVECTIN-7 for advanced metastatic melanoma died more than two months later of progressive disease and numerous other factors, after receiving multiple other cancer therapies. The death was originally reported as unrelated to the treatment. Following an autopsy, the death was reclassified as "probably related" to the treatment because the possibility could not be ruled out. We do not believe ALLOVECTIN-7 was a significant factor in the patient's death.

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

OUR PATENTS AND PROPRIETARY RIGHTS MAY NOT PROVIDE US WITH ANY BENEFIT AND THE PATENTS OF OTHERS MAY PREVENT US FROM COMMERCIALIZING OUR PRODUCTS.

Patents may not issue from any of our current applications. Moreover, if patents do issue, governmental authorities may not allow claims sufficient to protect our technology. Finally, others may challenge or seek to circumvent or invalidate patents that are issued to us or to licensors of our technology. In that event, the rights granted under patents may be inadequate to protect our proprietary technology or to provide any commercial advantage.

Our core DNA delivery technology is covered by a patent issued in Europe which is being opposed by several companies under European patent procedures. If we are not successful in this

Others may have or may receive patents which contain claims applicable to our products. These patents may impede our ability to commercialize products.

THE LEGAL PROCEEDINGS TO OBTAIN PATENTS AND LITIGATION OF THIRD-PARTY CLAIMS OF INTELLECTUAL PROPERTY INFRINGEMENT COULD REQUIRE US TO SPEND MONEY AND COULD IMPAIR OUR OPERATIONS.

Our success will depend in part on our ability to obtain patent protection for our products and processes both in the United States and in other countries. The patent positions of biotechnology and pharmaceutical companies, however, can be highly uncertain and involve complex legal and factual questions. Therefore, it is difficult to predict the breadth of claims allowed in the biotechnology and pharmaceutical fields.

We also rely on protecting our proprietary technology in part through confidentiality agreements with our corporate collaborators, employees, consultants and certain contractors. These agreements may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or independently discovered by our competitors.

Protecting intellectual property rights can be very expensive. Litigation may be necessary to enforce a patent issued to us or to determine the scope and validity of third-party proprietary rights. Moreover, if a competitor were to file a patent application claiming technology also invented by us, we would have to participate in an interference proceeding before the U.S. Patent and Trademark Office or in a foreign counterpart to determine the priority of the invention. We may be drawn into interferences with third parties or may have to provoke interferences ourselves to unblock third party patent rights so as to allow us or our licensees to commercialize products based on our technology. Litigation could result in substantial costs and the diversion of management's efforts regardless of the results of the litigation. An unfavorable result in litigation could subject us to significant liabilities to third parties, require disputed rights to be licensed or require us to cease using some technology.

Our products and processes may infringe, or be found to infringe on, patents not owned or controlled by us. We do not know whether any patents held by others will require us to alter our products or processes, obtain licenses, or stop activities. If relevant claims of third-party patents are upheld as valid and enforceable, we could be prevented from practicing the subject matter claimed in the patents, or may be required to obtain licenses or redesign our products or processes to avoid infringement. A number of genetic sequences or proteins encoded by genetic sequences that we are investigating are, or may become, patented by others. As a result, we may have to obtain licenses to test, use or market these products. Our business will suffer if we are not able to obtain licenses at all or on terms commercially reasonable to us and we may not be able to redesign our products or processes to avoid infringement.

COMPETITION AND TECHNOLOGICAL CHANGE MAY MAKE OUR POTENTIAL PRODUCTS AND TECHNOLOGIES LESS ATTRACTIVE OR OBSOLETE.

We compete with companies, including major pharmaceutical and biotechnology firms, that are pursuing other forms of treatment or prevention for the diseases we target. We also may experience competition from companies that have acquired or may acquire technology from universities and other research institutions. As these companies develop their technologies, they may develop proprietary positions which may prevent us from successfully commercializing products.

Some of our competitors are established companies with greater financial and other resources than we have. Other companies may succeed in developing products earlier than we do, obtaining FDA approval for products more rapidly than we do, or developing products that are more effective than those we propose to develop. While we will seek to expand our technological capabilities to remain competitive, research and development by others will seek to render our technology or products obsolete or noncompetitive or result in treatments or cures superior to any therapy developed by us. Additionally, consumers may not prefer therapies developed by us over existing or newly developed therapies.

THE METHOD OF ADMINISTRATION OF SOME OF OUR POTENTIAL PRODUCTS CAN CAUSE ADVERSE EVENTS IN PATIENTS, INCLUDING DEATH.

Some of our potential products are designed to be injected directly into malignant tumors. There are medical risks inherent in direct tumor injections. For example, in clinical trials of our potential products, attending physicians have punctured patients' lungs in less than one percent of procedures, requiring hospitalization. In addition, a physician

administering our product in an investigator-sponsored clinical trial inadvertently damaged tissue near the heart of a patient which may have precipitated the patient's death. These events are reported as adverse events in our clinical trials and illustrate the medical risks related to direct injection of tumors. These risks may adversely impact market acceptance of some of our products.

COMMERCIALIZATION OF SOME OF OUR POTENTIAL PRODUCTS DEPENDS ON COLLABORATIONS WITH OTHERS. IF OUR COLLABORATORS ARE NOT SUCCESSFUL OR IF WE ARE UNABLE TO FIND COLLABORATORS IN THE FUTURE, WE MAY NOT BE ABLE TO DEVELOP THESE PRODUCTS.

Our strategy for the research, development and commercialization of some of our product candidates requires us to enter into contractual arrangements with corporate collaborators, licensors, licensees and others. Our success depends upon the performance by these collaborators of their responsibilities under these arrangements. Some collaborators may not perform their obligations as we expect or we may not derive any revenue from these arrangements.

We have collaborative agreements with several pharmaceutical companies. We do not know whether these companies will successfully develop and market any products under their respective agreements. Moreover, some of our collaborators are also researching competing technologies to treat the diseases targeted by our collaborative programs. We may be unsuccessful in entering into other collaborative arrangements to develop and commercialize our products.

IF WE LOSE OUR KEY PERSONNEL OR ARE UNABLE TO ATTRACT AND RETAIN ADDITIONAL PERSONNEL, WE MAY NOT BE ABLE TO PURSUE COLLABORATIONS OR DEVELOP OUR OWN PRODUCTS.

We are highly dependent on the principal members of our scientific, manufacturing, marketing and management personnel, the loss of whose services might significantly delay or prevent the achievement of our objectives. We face competition from other companies, academic institutions, government entities and other organizations in attracting and retaining personnel.

WE MAY NOT BE ABLE TO MANUFACTURE PRODUCTS ON A COMMERCIAL SCALE.

We have limited experience in manufacturing our product candidates in commercial quantities. We may be dependent initially on corporate partners, licensees or others to manufacture our products commercially. We also will be required to comply with extensive regulations applicable to manufacturing facilities. We may be unable to enter into any arrangement for the manufacture of our products.

WE HAVE NO MARKETING OR SALES EXPERIENCE, AND IF WE ARE UNABLE TO DEVELOP OUR OWN SALES AND MARKETING CAPABILITY, WE MAY NOT BE SUCCESSFUL IN COMMERCIALIZING OUR PRODUCTS.

Our current strategy is to market our proprietary cancer products directly in the United States, but we currently do not possess pharmaceutical marketing or sales capabilities. In order to market and sell our proprietary cancer products, we will need to develop a sales force and a marketing group with relevant pharmaceutical experience, or make appropriate arrangements with strategic partners to market and sell these products. Developing a marketing and sales force is expensive and time consuming and could delay any product launch. Our inability to successfully employ qualified marketing and sales personnel and develop our sales and marketing capabilities will harm our business.

HEALTH CARE REFORM AND RESTRICTIONS ON REIMBURSEMENT MAY LIMIT OUR RETURNS ON POTENTIAL PRODUCTS.

Our ability to earn sufficient returns on our products will depend in part on the extent to which reimbursement for our products and related treatments will be available from:

- - government health administration authorities,

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- - private health coverage insurers,
- - managed care organizations, and
- - other organizations.

If we fail to obtain appropriate reimbursement, it could prevent us from successfully commercializing our potential products.

There are efforts by governmental and third party payors to contain or reduce the costs of health care through various means. We expect that there will continue to be a number of legislative proposals to implement government controls. The announcement of proposals or reforms could impair

our ability to raise capital. The adoption of proposals or reforms could impair our business.

Additionally third party payors are increasingly challenging the price of medical products and services. If purchasers or users of our products are not able to obtain adequate reimbursement for the cost of using our products, they may forego or reduce their use. Significant uncertainty exists as to the reimbursement status of newly approved health care products, and whether adequate third party coverage will be available.

WE USE HAZARDOUS MATERIALS IN OUR BUSINESS. ANY CLAIMS RELATING TO IMPROPER HANDLING, STORAGE OR DISPOSAL OF THESE MATERIALS COULD BE TIME CONSUMING AND COSTLY.

Our research and development processes involve the controlled storage, use and disposal of hazardous materials, biological hazardous materials and radioactive compounds. We are subject to federal, state and local regulations governing the use, manufacture, storage, handling and disposal of materials and waste products. Although we believe that our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by law and regulation, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated. In the event of an accident, we could be held liable for any damages that result, and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance on acceptable terms, or at all. We could be required to incur significant costs to comply with current or future environmental laws and regulations.

WE MAY HAVE SIGNIFICANT PRODUCT LIABILITY EXPOSURE.

We face an inherent business risk of exposure to product liability and other claims in the event that our technologies or products are alleged to have caused harm. These risks are inherent in the development of chemical and pharmaceutical products. Although we currently maintain product liability insurance, we may not have sufficient insurance coverage and we may not be able to obtain sufficient coverage at a reasonable cost. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the commercialization of any products developed by us or our collaborators. We also have liability for products manufactured by us on a contract basis for third parties. If we are sued for any injury caused by our technology or products, our liability could exceed our total assets.

OUR STOCK PRICE COULD CONTINUE TO BE HIGHLY VOLATILE AND YOU MAY NOT BE ABLE TO RESELL YOUR SHARES AT OR ABOVE THE PRICE YOU PAID FOR THEM.

The market price of our common stock, like that of many other life sciences companies, has been highly volatile and is likely to continue to be highly volatile. The following factors, among others, could have a significant impact on the market price of our common stock:

- - the results of our preclinical studies and clinical trials or those of our collaborators of competitors or for DNA therapeutics in general,
  - - evidence of the safety or efficacy of our potential products or the products of our competitors,
  - - the announcement by us or our competitors of technological innovations or new products,
  - - governmental regulatory actions,
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- - changes or announcements in reimbursement policies,
  - - developments with our collaborators,
  - - developments concerning our patent or other proprietary rights or those of our competitors, including litigation,
  - - concern as to the safety of our potential products,
  - - period-to-period fluctuations in our operating results,
  - - market conditions for life science stocks in general, and
  - - changes in estimates of our performance by securities analysts.

IF WE, OUR STRATEGIC PARTNERS OR OUR SUPPLIERS FAIL TO REMEDY YEAR 2000 ISSUES, OUR PRODUCT DEVELOPMENT PROGRAMS COULD BE INTERRUPTED AND OUR BUSINESS AND OPERATING RESULTS COULD BE HARMED.

If we, our strategic partners, or our suppliers of goods and services fail to remedy any Year 2000 issues, our business operations and development programs could be interrupted. Through March 1, 2000, we have not experienced any immediate adverse impacts related to the Year 2000, including the impacts of the Year 2000 being a leap year. However, there may be adverse events which have occurred but which are not yet apparent to us, our strategic partners and our suppliers. We will continue to monitor our Year 2000 compliance and that of our strategic partners and suppliers. Our costs for Year 2000 compliance have been immaterial. We do not believe that Year 2000 issues will have a material impact on our business, financial condition or results of operations.

OUR ANTI-TAKEOVER PROVISIONS COULD DISCOURAGE POTENTIAL TAKEOVER ATTEMPTS AND MAKE ATTEMPTS BY STOCKHOLDERS TO CHANGE MANAGEMENT MORE DIFFICULT.

The approval of two-thirds of our voting stock is required to approve some transactions and to take some stockholder actions, including the calling of a special meeting of stockholders and the amendment of any of the anti-takeover provisions contained in our certificate of incorporation. Further, pursuant to the terms of our stockholder rights plan adopted in March 1995, we have distributed a dividend of one right for each outstanding share of common stock. These rights will cause substantial dilution to the ownership of a person or group that attempts to acquire us on terms not approved by our Board of Directors and may have the effect of deterring hostile takeover attempts.

EXECUTIVE OFFICERS

The executive officers of Vical are elected annually by the Board of Directors. Our executive officers are as follows:

<TABLE>  
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NAME	AGE	POSITION
Alain B. Schreiber, M.D.	44	President, Chief Executive Officer and Director
Deirdre Y. Gillespie, M.D.	43	Executive Vice President and Chief Business Officer
Martha J. Demski Secretary	47	Vice President, Chief Financial Officer, Treasurer and Secretary
George J. Gray	53	Vice President, Operations
Jon A. Norman, Ph.D.	51	Vice President, Research
Robert H. Zaugg, Ph.D.	50	Vice President, Business Development

</TABLE>  
- -----

ALAIN B. SCHREIBER, M.D., has been our President, Chief Executive Officer and a director since May 1992. Prior to joining us, Dr. Schreiber held various executive level positions at Rhone-Poulenc Rorer Inc. from July 1985 to April 1992, lastly as Senior Vice President of Discovery Research. From October 1982 to June 1985, Dr. Schreiber served as Biochemistry Department Head at Syntex Corp. Dr. Schreiber is a director of Spiros Development Corp. II Inc. and is also an appointed adviser for foreign trade of the Belgian Foreign Trade Counsel in the United States. He received his undergraduate degree and M.D. from the Free University of Brussels, after which he was awarded a fellowship in immunology at the Weizmann Institute.

DEIRDRE Y. GILLESPIE, M.D., joined us as Executive Vice President and Chief Business Officer in March 1998. Prior to joining us, Dr. Gillespie served as Vice President of Business Development for 3-Dimensional Pharmaceuticals, Inc. From 1991 to 1996, she held various management positions with the Dupont Merck Pharmaceutical Co. From 1986 to 1990, Dr. Gillespie directed clinical research activities for Sandoz Pharma AG. Dr. Gillespie received a B.Sc. in Pharmacology and Therapeutics and an M.D. from London University. Dr. Gillespie received her M.B.A. from the London Business School with a specialization in marketing and international management.

MARTHA J. DEMSKI joined us as Chief Financial Officer in December 1988 and currently serves as Vice President, Chief Financial Officer, Treasurer and Secretary. From August 1977 until joining us, Ms. Demski held various positions with Bank of America, lastly as Vice President/Section Head of the Technology Section. She also served as an adviser to Bank of America on a statewide basis regarding the biotechnology industry in California. Ms. Demski received a B.A. from Michigan State University and an M.B.A. in Finance and Accounting from The University of Chicago Graduate School of Business.

JON A. NORMAN, PH.D., joined us in January 1993 as Vice President, Research. From 1986 until joining us, Dr. Norman was the Group Leader/Section Head for the Departments of Pharmacology and Biochemistry at Bristol-Myers Squibb Corporation. He was a Senior Research Scientist at Ciba-Geigy Corporation from 1981 to 1986. Dr. Norman received his B.A. and M.A. from the University of California at Santa Barbara and his Ph.D. in Biochemistry from the University of Calgary, after which he was awarded a fellowship at the Friederich Miescher Institute in Basel, Switzerland.

GEORGE J. GRAY joined us in October 1992 as Vice President, Operations. Prior to that time he was at Rhone-Poulenc Rorer Inc. where he held various positions since 1975, lastly as Director, Discovery Research Ventures, US/UK from January 1990 to October 1992, and prior to that as Director, Project Management from January 1988 to December 1989. Mr. Gray received a B.A. from George Washington University.

ROBERT H. ZAUGG, PH.D., joined us in July 1991 as the Senior Director, Business Development and has served as the Vice President of Business Development since January 1994. Prior to joining us, Dr. Zaugg served as Director of Business Development & Licensing for Triton Biosciences from 1988 to 1991 and in various business development positions with Sandoz Pharmaceuticals Corporation from 1982

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to 1988. He holds a B.A. from the University of California at Los Angeles, a Ph.D. in Biochemistry from Northwestern University and an M.B.A. from New York University. He was awarded a post-doctoral fellowship in immunology at the Massachusetts Institute of Technology.

ITEM 2. PROPERTIES

Vical currently leases approximately 43,000 square feet of laboratory and office space in San Diego, California, at three sites and with three leases. The leases terminate in 2004 and contain varying renewal options. Total current monthly rental on the facilities, including common area maintenance costs, is approximately \$107,000.

ITEM 3. LEGAL PROCEEDINGS

Not applicable.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Vical's common stock is traded on the Nasdaq National Market under the symbol "VICL." The following table presents quarterly information on the price range of high and low sales prices for the common stock on the Nasdaq National Market for the periods indicated since January 1, 1998.

<TABLE>  
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1998	HIGH	LOW
First Quarter	\$18.00	\$12.00
Second Quarter	19.00	14.00
Third Quarter	17.88	7.19
Fourth Quarter	18.00	8.00
1999		
First Quarter	\$17.00	\$10.00
Second Quarter	13.50	9.13
Third Quarter	16.66	10.88
Fourth Quarter	30.13	13.13

</TABLE>

As of March 15, 2000, there were approximately 516 stockholders of record of Vical common stock with 19,814,986 shares outstanding. We have never declared or paid any dividends and do not expect to pay any dividends in the foreseeable future.

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ITEM 6. SELECTED FINANCIAL DATA

<TABLE>  
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YEAR ENDED DECEMBER 31,

-----  
1999                      1998                      1997                      1996                      1995

	(in thousands, except per share and share amounts)				
<S>	<C>	<C>	<C>	<C>	<C>
STATEMENT OF OPERATIONS DATA:					
Revenues:					
License/royalty revenue.....	\$ 8,294	\$ 5,044	\$ 6,477	\$ 5,679	\$ 5,402
	\$ 2,417	\$ 876	\$ 1,326	\$ 1,061	\$ 900
Contract revenue.....	10,711	5,920	7,803	6,740	6,302
Operating expenses:					
Research and development...	15,344	12,054	11,936	11,318	8,997
General and administrative.	4,376	3,650	3,733	3,168	2,902
Total operating expenses	19,720	15,704	15,669	14,486	11,899
Loss from operations.....	(9,009)	(9,784)	(7,866)	(7,746)	(5,597)
Interest income.....	2,229	2,465	2,447	2,773	1,687
Interest expense.....	129	162	192	108	73
Net loss.....	\$ (6,909)	\$ (7,481)	\$ (5,611)	\$ (5,081)	\$ (3,983)
Net loss per share (basic and diluted) .....	\$ (0.43)	\$ (0.47)	\$ (0.36)	\$ (0.33)	\$ (0.29)
Shares used in per share calculation.....	16,135,590	15,797,585	15,484,952	15,382,848	13,504,790

</TABLE>  
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	AS OF DECEMBER 31,				
<S>	1999	1998	1997	1996	1995
<C>	<C>	<C>	<C>	<C>	<C>
BALANCE SHEET DATA:					
Cash, cash equivalents and marketable securities.....	\$ 37,675	\$ 40,184	\$ 45,555	\$ 46,846	\$ 52,528
Working capital.....	35,996	38,398	44,856	46,315	51,541
Total assets.....	45,059	44,844	50,691	52,440	55,118
Long-term obligations.....	740	801	1,232	1,617	339
Stockholders' equity.....	38,669	40,824	47,194	48,365	53,264

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

OVERVIEW

We were incorporated in April 1987 and have devoted substantially all of our resources since that time to our research and development programs. We focus our resources on the development of our naked DNA direct gene transfer and related technologies. We are developing our ALLOVECTIN-7, LEUVECTIN and VAXID cancer product candidates internally, while developing vaccine product candidates for infectious diseases primarily in collaboration with corporate partners Merck, and Aventis Pasteur, formerly Pasteur Merieux Connaught. We have a license agreement allowing Centocor to use our naked DNA technology to develop and market gene-based vaccines for the potential treatment of types of cancer. We have an agreement with Boston Scientific for the use of our technology in catheter-based intravascular gene delivery. We have an agreement with Aventis Pharma, formerly Rhone-Poulenc Rorer, to use our gene delivery technology to deliver neurological proteins for neurodegenerative diseases. We also have agreements with Pfizer for use of our technology for DNA-based delivery of therapeutic proteins in animal health applications and with Merial for use of our technology for DNA vaccines in animal infectious disease targets. In February 2000, the Company and Human Genome Sciences, Inc. (HGS) signed a reciprocal royalty-bearing license. Under the agreement, Vical has the option to exclusively license up to

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three genes from HGS for gene-based product development. HGS has the option to license Vical's naked DNA gene delivery technology for use in up to three gene-based products. In addition, we granted an exclusive, royalty-bearing license to Vascular Genetics Inc. (VGI), a company in which HGS is a major shareholder, for naked DNA delivery of a gene with potential use for revascularization.

To date, we have not received revenues from the sale of products. We expect to incur substantial operating losses for at least the next few years, due primarily to the expansion of our research and development programs and the cost of preclinical studies and clinical trials. Losses may fluctuate from quarter to quarter as a result of differences in the timing of expenses incurred and the revenues received from collaborative agreements. Such fluctuations may



be significant. As of December 31, 1999, our accumulated deficit was approximately \$44.6 million.

When used in this discussion, the words "expects," "anticipated" and similar expressions are intended to identify forward-looking statements. These statements are subject to risks and uncertainties which could cause actual results to differ materially from those projected. Readers are cautioned not to place undue reliance on these forward-looking statements which speak only as of the date of this report. We undertake no obligation to publicly release the result of any revisions to these forward-looking statements which may be made to reflect events or circumstances after the date of this report to reflect the occurrence of unanticipated events.

#### RESULTS OF OPERATIONS

Vical had revenues of \$10.7 million for the year ended December 31, 1999, compared with \$5.9 million in 1998 and \$7.8 million in 1997. License revenue in 1999 included \$2.0 million from Merck to extend an agreement covering therapeutic naked DNA vaccines and \$1.0 million for the start of a Phase I clinical trial of a preventive naked DNA vaccine to protect against HIV infection; \$1.0 million of option fees and \$1.2 million of equity premium pursuant to January 1999 agreements with Pfizer Inc.; and \$1.0 million from Merial for the initial exercise of options covering preventive naked DNA vaccines for animal health infectious diseases. The equity premium from Pfizer was a result of Pfizer purchasing for \$6.0 million approximately 318,000 shares of Vical common stock at \$18.87 per share. The price per share reflected a twenty-five percent premium over the trading price of the common stock. The equity premium was recognized as license revenue in 1999. License revenue also included recognition of previously deferred license fees of \$1.1 million from Merial, and royalty and other revenue of \$1.0 million. Contract revenues for 1999 were \$2.4 million, primarily from the Office of Naval Research for the development work on a potential DNA vaccine to prevent malaria and payments under the January 1999 agreement with Pfizer to fund research and development of up to \$500,000 per year for three years.

Vical had revenues of \$5.9 million for the year ended December 31, 1998. License revenues in 1998 consisted of \$2.2 million from Centocor, Inc. for an agreement covering technology for the potential treatment of some types of cancer, \$1.1 million from an agreement with Boston Scientific Corporation for the development of catheter-based vascular DNA therapeutics, recognition of \$0.9 million of deferred license fees from a further extension of the license and option agreement with Merial, and royalty and other revenues of \$0.9. Contract revenues in 1998 consisted principally of \$0.7 million from the Office of Naval Research.

Vical had revenues of \$7.8 million for the year ended December 31, 1997. License revenues in 1997 were composed of \$2.0 million from a 1997 Merck agreement covering certain growth factors; the equity premium of \$1.0 million on the investment Merck made in 1997 in Vical common stock under an amendment to the 1991 collaborative agreement; \$1.3 million for the Aventis Pasteur collaboration; \$1.0 million for a 1997 collaborative agreement with Aventis Pharma for neurodegenerative disease targets; and royalties, amortization of deferred license fees from Merial and other revenue which totaled \$1.2 million. In November 1997, Vical and Merck amended the 1991 agreement and granted Merck rights to develop and market therapeutic vaccines against HIV and HBV. Under the November 1997 amendment, Merck made an investment of \$5.0 million for approximately 262,000 shares of Vical common stock. The price per share reflected a twenty-five percent premium over the trading price of the common stock. The premium on the investment was reflected in revenue in 1997. License revenue from Aventis Pasteur of \$1.3 million represented \$1.0 million for a milestone payment for the start of the malaria clinical trial and the balance was the recognition of deferred license fees. Contract revenue in 1997 primarily represented \$1.1 million as payment from Aventis Pasteur for clinical and preclinical work.

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In December 1999, the SEC issued Staff Accounting Bulletin No. 101 - "Revenue Recognition" (SAB 101). SAB 101 reflects the SEC's views on revenue recognition. Historically we have recognized revenue from initial option and license fees in the period in which the agreement was signed if there were no significant performance obligations remaining. Revenue from milestone payments was recognized as revenue when the milestones were achieved. SAB 101 would require that revenue from option and license fees and milestone payments be deferred and recognized over the period of the option or license agreement. Companies which have not adhered to the guidance in SAB 101 will be required to reflect a cumulative effect adjustment of a change in accounting principle in their financial statements for the first fiscal quarter of the fiscal year beginning after December 15, 1999. We have not completed our evaluation of the impact of SAB 101 on our financial statements, however, the potential impact is expected to be material to the financial statements.

Research and development expense increased to \$15.3 million in 1999 from \$12.1 million in 1998 and \$11.9 million in 1997. The increases in

research and development expense were generally due to expansion of our research and development activities. The increase in expenses in 1999 compared to 1998 included increased clinical and preclinical efforts which resulted in increases to clinical trials expense, staffing costs, external research and contract services. The increase in 1998 compared to 1997 principally was due to increased clinical trial costs and additional royalty expense for license agreements. Clinical trials expense increased to \$3.6 million during 1999 from \$1.9 million in 1998. This increase mostly was due to increased activity in ALLOVECTIN-7 clinical trials. Clinical trials expense increased to \$1.9 million during 1998 from \$1.6 million in 1997 primarily due to the commencement of the Phase II and Phase III clinical trials of ALLOVECTIN 7 for melanoma. Research and development expense is expected to increase as our preclinical and clinical trial activities increase.

General and administrative expense increased to \$4.4 million in 1999 from \$3.6 million during 1998 primarily due to additional staffing and related expenses. The decrease in general and administrative expense to \$3.6 million in 1998 from \$3.7 million in 1997 is due to lower insurance and facilities expenses. General and administrative expenses are expected to continue to increase as research and development activities expand.

Interest income decreased to \$2.2 million in 1999 from \$2.5 million in 1998 due to lower average balances of investments and lower rates of return on investments. Interest income of \$2.5 million during 1998 increased from \$2.4 million in 1997, due to higher rates of return on investments. Interest expense decreased during 1999 compared to 1998, and during 1998 compared to 1997, due to lower average balances of capital lease obligations and a bank note payable. Interest income is expected to increase in 2000 compared to 1999 due to the sale of 3,450,000 shares of common stock in January 2000 for net proceeds of approximately \$117.5 million.

#### LIQUIDITY AND CAPITAL RESOURCES

Since its inception, Vical has financed its operations primarily through private placements of common stock and preferred stock, four public offerings of common stock (including an offering completed in January 2000), and revenues from collaborative agreements. As of December 31, 1999, we had working capital of approximately \$36.0 million compared with \$38.4 million at December 31, 1998. Cash and marketable securities totaled approximately \$37.7 million at December 31, 1999, compared with \$40.2 million at December 31, 1998. On January 20, 2000, Vical sold 3,450,000 shares of common stock, including an over-allotment to the underwriters of 450,000 shares, in a public offering for \$36.50 per share. Net proceeds to Vical were approximately \$117.5 million after deducting underwriting fees and offering costs. In November 1999, we entered into an unsecured line of credit with a bank to provide financing for leasehold improvements. Under the terms of the agreement, we may borrow up to \$1.0 million through May 1, 2000. No borrowings were outstanding under this agreement at December 31, 1999.

We expect to incur substantial additional research and development expenses and general and administrative expenses, including continued increases in personnel costs, costs related to preclinical testing and clinical trials, outside services and facilities. Our future capital requirements will depend on many factors, including continued scientific progress in our research and development programs, the scope and results of preclinical testing and clinical trials, the time and costs involved in obtaining regulatory approvals, the costs involved in filing, prosecuting and enforcing patent claims, competing

technological and market developments, the cost of manufacturing scale-up, and commercialization activities and arrangements. We intend to seek additional funding through research and development relationships with suitable potential corporate collaborators. We may also seek additional funding through public or private financings. We cannot assure that additional financing will be available on favorable terms or at all.

If additional funding is not available, we anticipate that, including the net proceeds from the January stock offering, our available cash and existing sources of funding will be adequate to satisfy our operating needs through at least 2002.

#### YEAR 2000 ISSUES

Through March 1, 2000, we have not experienced any immediate adverse impacts related to the Year 2000, including the impacts of the Year 2000 being a leap year. However, there may be adverse events which have occurred but which are not yet apparent to us, our strategic partners and our suppliers. We will continue to monitor our Year 2000 compliance and that of our collaborators and suppliers. Our costs for Year 2000 compliance have been immaterial. We do not believe that Year 2000 issues will have a material impact on our business, financial condition or results of operations.

ITEM 7.a. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

We are subject to interest rate risk. Vical's investment portfolio is maintained in accordance with our investment policy which defines allowable investments, specifies credit quality standards and limits the credit exposure of any single issuer. No investments in equity securities are made. At December 31, 1999, 75 percent of the investments would mature within one year and 25 percent would mature within two years, and the average maturity was nine months. Our investments are all classified as available-for-sale securities. We projected an ending fair value of our cash equivalents and marketable securities using a twelve-month time horizon, a nine-month average maturity and assuming a 150-basis-point increase in interest rates. The decrease in fair value assuming a 150-basis-point increase in interest rates compared with fair value with no change in interest rates was not material at December 31, 1999. In January 2000, Vical sold 3,450,000 shares of common stock, including an over-allotment to the underwriters of 450,000 shares, in a public offering for \$36.50 per share. Net proceeds to Vical were approximately \$117.5 million after deducting underwriting fees and offering costs. Including the \$117.5 million net proceeds from the stock offering together with the marketable securities balance at December 31, 1999 and using the same assumptions as previously described, would result in a pro forma potential unrealized decrease of \$0.5 million compared with a pro forma carrying value of these investments of approximately \$162.3 million.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The consolidated financial statements and supplementary data of Vical required by this item are set forth at the pages indicated in Item 14(a)(1).

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS

DIRECTORS

The directors of Vical are as follows:

<TABLE> <CAPTION> NAME	AFFILIATION
- ----	-----
<S>	<C>
R. Gordon Douglas	Chairman of the Board, Vical Incorporated
Alain B. Schreiber, M.D.	President and CEO, Vical Incorporated

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M. Blake Ingle	Inglewood Ventures
Patrick F. Latterell	Venrock Associates
Gary A. Lyons	Neurocrine Biosciences, Inc.
Dale A. Smith	Baxter International Inc. (retired)
Philip M. Young	U.S. Venture Partners

The information required by this item (with respect to Directors) is incorporated by reference from the information under the caption "Election of Directors" contained in Vical's Proxy Statement to be filed with the Securities and Exchange Commission in connection with the solicitation of proxies for Vical's 2000 Annual Meeting of Stockholders to be held on May 18, 2000 ("Proxy Statement"). The required information concerning Executive Officers of Vical is contained in Part I of this Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference from the information under the caption "Executive Compensation" contained in the Proxy Statement.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this item is incorporated by reference from the information under the caption "Security Ownership of Certain Beneficial Owners and Management" contained in the Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required by this item is incorporated by reference from

the information contained under the caption "Certain Transactions" contained in the Proxy Statement.

PART IV

ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K

(a) (1) FINANCIAL STATEMENTS

The financial statements required by this item are submitted in a separate section beginning on page F-1 of this report.

<TABLE>  
<CAPTION>

FINANCIAL STATEMENTS	
-----	
<S>	<C>
Report of Independent Public Accountants	F-1
Balance Sheets at December 31, 1999 and 1998	F-2
Statements of Operations for the three years ended December 31, 1999	F-3
Statements of Stockholders' Equity for the three years ended December 31, 1999	F-4
Statements of Cash Flows for the three years ended December 31, 1999	F-5
Notes to Financial Statements	F-6

</TABLE>

(2) FINANCIAL STATEMENT SCHEDULES

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Schedules have been omitted because of the absence of conditions under which they are required or because the required information is included in the financial statements or the notes thereto.

(3) EXHIBITS

Exhibits with each management contract or compensatory plan or arrangement required to be filed are identified. See paragraph (c) below.

(b) REPORTS ON FORM 8-K

No reports on Form 8-K were filed during the quarter ended December 31, 1999.

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(c) EXHIBITS

<TABLE>  
<CAPTION>

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
-----	-----
<S>	<C>
3.1(i)(9)	Restated Certificate of Incorporation.
3.1(ii)(9)	Amended and Restated Bylaws of the Company.
4.1(9)	Specimen Common Stock Certificate.
4.2(2)	Rights Agreement dated as of March 20, 1995, between the Company and First Interstate Bank of California.
4.3(10)	Stock Purchase Agreement dated November 3, 1997, between the Company and Merck & Co., Inc.
4.4(11)	Stock Purchase Agreement dated as of January 22, 1999, between the Company and Pfizer Inc.
10.1(4)#	Stock Incentive Plan of Vical Incorporated.
10.2(5)#	1992 Directors' Stock Option Plan of Vical Incorporated.
10.3(3)	Form of Indemnity Agreement between the Company and its directors and officers.
10.5(3)#	Employment Agreement dated August 20, 1992, between the Company and

	Mr. George J. Gray.
10.6(3)#	Employment Agreement dated November 2, 1992, between the Company and Dr. Jon A. Norman.
10.7(3)	Stock Purchase Agreement dated February 20, 1992.
10.8(3)	Lease dated December 4, 1987, between the Company and Nexus/GADCo.-UTC, a California Joint Venture, as amended.
10.9(6)*	Research Collaboration and License Agreement dated May 31, 1991, between the Company and Merck & Co., Inc.
10.12(1)*	License Agreement dated January 1, 1991, between the Company and Wisconsin Alumni Research Foundation.
10.14(1)*	License Agreement dated October 23, 1992, between the Company and the Regents of University of Michigan.
10.16(7)	Research, Option and License Agreement dated September 29, 1994, between the Company and Pasteur Merieux Serums & Vaccins.
10.17(8)	Amendment dated April 27, 1994, to Research Collaboration and License Agreement dated May 31, 1991, between the Company and Merck & Co., Inc.
10.19(10)*	Amendment dated November 3, 1997, to Research Collaboration and License Agreement dated May 31, 1991, between the Company and Merck & Co., Inc.
10.20(12)	Amendment No. 4 to the Lease dated December 4, 1987, between the Company and Nippon Landic (U.S.A.), Inc., a Delaware Corporation (as successor in interest to Nexus GADGO-UTC)
23.1	Consent of Arthur Andersen LLP.
27	Financial Data Schedule

</TABLE>

- 
- (1) Incorporated by reference to the Company's Registration Statement on Form S-1 (No. 33-56830) filed on January 7, 1993.
  - (2) Incorporated by reference to the exhibit of the same number to the Company's Report on Form 10-K for the Fiscal Year ended December 31, 1994 (No. 0-21088).
  - (3) Incorporated by reference to the Exhibits of the same number filed with the Company's Registration Statement on Form S-1 (No. 33-56830) filed on January 7, 1993.
  - (4) Incorporated by reference to Exhibit 10.1 filed with the Company's Registration Statement on Form S-8 (file No. 333-80681) filed on June 15, 1999.
  - (5) Incorporated by reference to Exhibit 10.1 filed with the Company's Registration Statement on Form S-8 (No. 333-30181) filed on June 27, 1997.
  - (6) Incorporated by reference to Exhibit 10.9 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 1994 (No. 0-21088).

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- (7) Incorporated by reference to Exhibit A of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 1994.
- (8) Incorporated by reference to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 1994 (No. 0-21088).
- (9) Incorporated by reference to the exhibit of the same number filed with the Company's Registration Statement on Form S-3 (No. 33-95812) filed on August 15, 1995.
- (10) Incorporated by reference to the exhibit of the same number to the Company's Annual Report on Form 10-K for the year ended December 31, 1997, filed on March 30, 1998.
- (11) Incorporated by reference to the exhibit of the same number to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 1999.
- (12) Incorporated by reference to the exhibit of the same number to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999.

\* The Company has received confidential treatment of certain portions of these agreements.

# Indicates management contract or compensatory plan or arrangement.

(d) FINANCIAL STATEMENT SCHEDULES

The financial statement schedules of Vical Incorporated required by this item are set forth at the pages indicated in Item 14(a)(2).

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on March 23, 2000.

VICAL INCORPORATED

By: /s/ ALAIN B. SCHREIBER, M.D.  
-----  
Alain B. Schreiber, M.D.  
President and Chief Executive Officer

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.

<S>	<C>	<C>
/s/ ALAIN B. SCHREIBER, M.D. ----- Alain B. Schreiber, M.D.	President, Chief Executive Officer and Director	March 23, 2000
/s/ MARTHA J. DEMSKI ----- Martha J. Demski	Vice President, Finance Chief Financial Officer Secretary and Treasurer	March 23, 2000
/s/ R. GORDON DOUGLAS ----- R. Gordon Douglas	Chairman of the Board of Directors	March 23, 2000
/s/ PHILIP M. YOUNG ----- Philip M. Young	Director	March 23, 2000
/s/ PATRICK F. LATTERELL ----- Patrick F. Latterell	Director	March 23, 2000
/s/ DALE A. SMITH ----- Dale A. Smith	Director	March 23, 2000
/s/ M. BLAKE INGLE ----- M. Blake Ingle	Director	March 23, 2000
/s/ GARY A. LYONS ----- Gary A. Lyons	Director	March 23, 2000

REPORT OF INDEPENDENT PUBLIC ACCOUNTANTS

To Vical Incorporated:

We have audited the accompanying balance sheets of Vical Incorporated, a Delaware corporation, as of December 31, 1999 and 1998, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 1999. 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 auditing standards generally accepted in the 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 Vical Incorporated as of December 31, 1999 and 1998, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 1999, in conformity with accounting principles generally accepted in the United States.

ARTHUR ANDERSEN LLP

San Diego, California  
February 10, 2000, except with respect to the matter discussed in Note 10 for which the date is February 24, 2000

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VICAL INCORPORATED  
BALANCE SHEETS

<TABLE>  
<CAPTION>

	December
31,	1999
1998	-----
	--
	<C>
ASSETS	
Current Assets:	
Cash and cash equivalents	\$ 11,149,587
\$ 13,567,817	
Marketable securities - available-for-sale	26,525,181
26,615,939	
Receivables and other	3,971,621
1,432,711	
	-----
	--
Total current assets	41,646,389
41,616,467	
	-----
	--
Property and Equipment:	
Equipment	5,948,458
5,139,944	
Leasehold improvements	1,646,023
1,558,554	
	-----
	--
	7,594,481
6,698,498	
Less--accumulated depreciation and amortization	(5,708,349)
(4,992,121)	
	-----
	--
	1,886,132
1,706,377	
	-----
	--
Patent costs, net of accumulated amortization of \$220,715 and	
\$126,638	1,380,245
1,387,936	
Other assets	146,470
133,385	
	-----
	--
	\$ 45,059,236
\$ 44,844,165	
	=====
	--

LIABILITIES AND STOCKHOLDERS' EQUITY

Current Liabilities:

Accounts payable and accrued expenses	\$ 3,839,642
\$ 2,281,252	
Current portion of capital lease obligations	627,957
473,466	

Current portion of notes payable	106,887	
213,773		
Deferred revenue	1,076,166	
250,000		
-----		--
Total current liabilities	5,650,652	
3,218,491		
-----		--
Long-Term Obligations:		
Long-term obligations under capital leases	739,885	
747,807		
Notes payable	-	
53,443		
-----		--
Total long-term obligations	739,885	
801,250		
=====		
Commitments		
Stockholders' Equity:		
Preferred stock, \$.01 par value--5,000,000 shares authorized-- none outstanding	-	
-		
Common stock, \$.01 par value--40,000,000 shares authorized-- 158,665	162,011	
16,201,136 and 15,866,544 shares issued and outstanding in 1999 and 1998, respectively		
Additional paid-in capital	83,292,870	
78,332,483		
Accumulated other comprehensive income (loss)	(140,801)	
69,440		
Accumulated deficit	(44,645,381)	
(37,736,164)		
-----		--
Total stockholders' equity	38,668,699	
40,824,424		
-----		--
	\$ 45,059,236	
\$ 44,844,165		
=====		

</TABLE>

See accompanying notes.

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VICAL INCORPORATED  
STATEMENTS OF OPERATIONS

<TABLE>  
<CAPTION>

	Year ended December 31,		
	1999	1998	1997
-----	-----	-----	-----
<S>	<C>	<C>	<C>
Revenues:			
License/Royalty revenue	\$ 8,294,283	\$ 5,044,607	\$
6,477,244			
Contract revenue	2,417,198	875,773	
1,325,925			
-----	-----	-----	-----
	10,711,481	5,920,380	
7,803,169			
-----	-----	-----	-----
Operating expenses:			
Research and development	15,343,586	12,054,367	
11,936,068			
General and administrative	4,376,471	3,649,841	



3,733,290			
-----			
15,669,358	19,720,057	15,704,208	
-----			
Loss from operations (7,866,189)	(9,008,576)	(9,783,828)	
Other income (expense):			
Interest income	2,229,181	2,465,545	
2,447,139			
Interest expense	(129,822)	(162,224)	
(192,181)			
-----			
Net loss (5,611,231)	\$ (6,909,217)	\$ (7,480,507)	\$
=====			
Net loss per share (basic and diluted) (0.36)	\$ (0.43)	\$ (0.47)	\$
=====			
Weighted average shares used in computing net loss per share 15,484,952	16,135,590	15,797,585	
=====			

</TABLE>

See accompanying notes.

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VICAL INCORPORATED  
STATEMENTS OF STOCKHOLDERS' EQUITY  
FOR THE THREE YEARS ENDED DECEMBER 31, 1999

Accumulated Comprehensive Income	Common Stock		Additional	Other
	Shares	Amount	Paid-in Capital	
-----				
<S>	<C>	<C>	<C>	<C>
BALANCE, December 31, 1996 (48,785)	15,396,582	\$ 153,966	\$ 72,904,472	\$
Issuance of common stock	261,812	2,618	3,992,143	
-				
Stock option exercises	72,922	729	371,356	
-				
Unrealized gain on marketable securities arising during holding period				
Reclassification of realized loss included in net loss				
Unrealized gain on marketable securities	-	-	-	
72,813				
Net loss	-	-	-	
-				
-----				
BALANCE, December 31, 1997 24,028	15,731,316	157,313	77,267,971	
Stock option exercises	135,228	1,352	1,064,512	
-				
Unrealized gain on marketable securities arising during holding period				
Reclassification of realized gain included in net loss				
Unrealized gain on marketable securities	-	-	-	
45,412				

Net loss	-	-	-	
-----				
BALANCE, December 31, 1998 69,440	15,866,544	158,665	78,332,483	
Issuance of common stock	317,969	3,180	4,790,461	
Stock option exercises	16,623	166	169,926	
-----				
Unrealized loss on marketable securities arising during holding period				
Reclassification of realized gain included in net loss				
Unrealized loss on marketable securities (210,241)	-	-	-	
Net loss	-	-	-	
-----				
BALANCE, December 31, 1999 (140,801)	16,201,136	\$ 162,011	\$ 83,292,870	\$
=====				

</TABLE>

<TABLE>  
<CAPTION>

	Accumulated Deficit	Total Stockholders' Equity	Total Comprehensive Loss	
	-----	-----	-----	
<S> BALANCE, December 31, 1996	<C> \$ (24,644,426)	<C> \$ 48,365,227	<C>	
Issuance of common stock	-	3,994,761		
Stock option exercises	-	372,085		
Unrealized gain on marketable securities arising during holding period			\$ 87,763	
Reclassification of realized loss included in net loss			(14,950)	
Unrealized gain on marketable securities	-	72,813	72,813	
Net loss	(5,611,231)	(5,611,231)	(5,611,231)	
-----				
BALANCE, December 31, 1997	(30,255,657)	47,193,655	\$ (5,538,418)	
=====				
Stock option exercises	-	1,065,864		
Unrealized gain on marketable securities arising during holding period			\$ 57,041	
Reclassification of realized gain included in net loss			(11,629)	
Unrealized gain on marketable securities	-	45,412	45,412	
Net loss	(7,480,507)	(7,480,507)	(7,480,507)	
-----				
BALANCE, December 31, 1998	(37,736,164)	40,824,424	\$ (7,435,095)	
=====				
Issuance of common stock	-	4,793,641		
Stock option exercises	-	170,092		
Unrealized loss on marketable securities arising during holding period			\$ (191,191)	
Reclassification of realized gain included in net loss			(19,050)	
Unrealized loss on marketable securities	-	(210,241)	(210,241)	
Net loss	(6,909,217)	(6,909,217)	(6,909,217)	
-----				
BALANCE, December 31, 1999	\$ (44,645,381)	\$ 38,668,699	\$ (7,119,458)	
=====				

</TABLE>

See accompanying notes.

<TABLE>  
<CAPTION>

	Year ended December 31,		
	1999	1998	1997
<S>	<C>	<C>	<C>
OPERATING ACTIVITIES:			
Net loss	\$ (6,909,217)	\$ (7,480,507)	\$ (5,611,231)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,041,351	920,695	939,956
Write-off of abandoned patent application costs	-	94,800	80,994
Changes in operating assets and liabilities:			
Receivables and other	(2,538,910)	133,821	359,463
Accounts payable and accrued expenses	1,558,390	856,649	614,219
Deferred revenue	826,166	71,739	(1,013,043)
Net cash used in operating activities	(6,022,220)	(5,402,803)	(4,629,642)
INVESTING ACTIVITIES:			
Marketable securities	(119,482)	6,826,955	912,645
Capital expenditures	(441,324)	(34,292)	(418,507)
Other assets	(13,086)	(1,885)	210,400
Patent expenditures	(86,386)	(288,252)	(280,778)
Net cash provided from (used in) investing activities	(660,278)	6,502,526	423,760
FINANCING ACTIVITIES:			
Principal payments under capital lease obligations	(539,136)	(487,702)	(506,205)
Payments on notes payable	(160,329)	(267,217)	(106,887)
Issuance of common stock, net	4,963,733	1,065,864	4,366,846
Net cash provided from financing activities	4,264,268	310,945	3,753,754
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	(2,418,230)	1,410,668	(452,128)
CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD	13,567,817	12,157,149	12,609,277
CASH AND CASH EQUIVALENTS AT END OF PERIOD	\$ 11,149,587	\$ 13,567,817	\$ 12,157,149
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Interest Paid	\$ 128,411	\$ 167,622	\$ 184,191
NONCASH INVESTING AND FINANCING ACTIVITIES:			
Equipment acquired under capital leases	\$ 685,705	\$ 348,920	\$ 434,416

</TABLE>

See accompanying notes.

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VICAL INCORPORATED  
NOTES TO FINANCIAL STATEMENTS  
December 31, 1999

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

ORGANIZATION AND BUSINESS ACTIVITY

Vical Incorporated (the "Company"), a Delaware corporation, was incorporated in 1987 and has devoted substantially all of its resources since that time to its research and development programs. The Company is focusing its resources on the development of its DNA gene transfer technologies for the prevention and treatment of life-threatening diseases.

All of the Company's potential products are in research and development. No revenues have been generated from the sale of any of such products, nor are any such revenues expected for at least the next few years. The products currently under development by the Company will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercial use. There can be no assurance that the Company's research and development efforts will be successful and that any of the Company's potential products will prove to be safe and effective in clinical trials. Even if developed, these products may not receive regulatory approval or be successfully introduced and marketed at prices that would permit the Company to operate profitably. The

Company expects to continue to incur substantial losses and not generate positive cash flow from operations for at least the next few years. No assurance can be given that the Company can generate sufficient product revenue to become profitable or generate positive cash flow from operations at all or on a sustained basis.

#### USE OF ESTIMATES

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

#### PROPERTY AND EQUIPMENT

Equipment is stated at cost and depreciated over the estimated useful lives of the assets (3-5 years) using the straight-line method. Leasehold improvements are stated at cost and amortized over the shorter of the life of the lease or the remaining useful life of the asset using the straight-line method.

#### PATENT COSTS

The Company capitalizes certain costs related to patent applications. Accumulated costs are amortized over the estimated economic lives of the patents using the straight-line method, commencing at the time the patents are issued. Costs related to patent applications are written off to expense at the time such costs are deemed to have no continuing value.

#### RESEARCH AND DEVELOPMENT COSTS

All research and development costs are expensed as incurred.

#### REVENUE UNDER COLLABORATIVE AGREEMENTS

The Company earns revenue from licensing access to its proprietary technology and performing services under research and development contracts. Initial fees under license and option agreements are recognized upon contract signing if the fee is nonrefundable and there are no significant performance obligations remaining. Fees to extend an option on the technology are recognized over the option extension period. Revenue from milestones is recognized as the milestones are achieved. Revenue under research and development contracts is recognized as the services are performed. Advance payments received in excess of amounts earned are classified as deferred revenue.

#### NET LOSS PER SHARE

Basic and diluted net loss per share for each of the three years in the period ended December 31, 1999, has been computed using the weighted average number of shares of common stock outstanding during the periods pursuant to Statement of Financial Accounting Standards No. 128, "Earnings Per Share." Diluted loss per share

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does not include any stock options as the effect would be antidilutive. See Note 6 for information on the number of options outstanding and the weighted average exercise price at December 31, 1999, 1998 and 1997.

#### INCOME TAXES

The Company accounts for income taxes in accordance with Statement of Financial Accounting Standards No. 109 ("SFAS 109"), "Accounting for Income Taxes."

#### FAIR VALUE OF FINANCIAL INSTRUMENTS

The carrying amounts of financial instruments such as accounts receivable, accounts payable and accrued expenses reasonably approximate fair value because of the short maturity of these items. The Company believes the carrying amounts of the Company's notes payable and obligations under capital leases approximate fair value because the interest rates on these instruments change with, or approximate, market interest rates.

#### COMPREHENSIVE INCOME (LOSS)

The Company has implemented Statement of Financial Accounting Standards No. 130 ("SFAS 130"), "Reporting Comprehensive Income." This statement requires that all items that are required to be recognized under accounting standards as components of comprehensive income be reported in a financial statement that is displayed with the same prominence as other financial statements. Accordingly, in addition to reporting net income (loss), the Company has displayed the impact of any unrealized gain or loss on marketable securities as a component of comprehensive income and has displayed an amount representing total comprehensive income (loss) for each period presented. The Company has presented the required information in the Statements of Stockholders' Equity.

**CAPITALIZED COSTS OF INTERNALLY DEVELOPED SOFTWARE** The Company has adopted AICPA Statement of Position 98-1, "Accounting for the Costs of Computer Software Developed or Obtained for Internal Use." This statement provides guidance on accounting for the costs of computer software developed or

obtained for internal use. The statement identifies characteristics of internal use software and assists in determining when computer software is for internal use. Implementation of this statement in 1999 did not have a material impact on the Company's financial statements.

#### BUSINESS SEGMENTS

The Company has adopted Statement of Financial Accounting Standards No. 131, "Disclosures about Segments of an Enterprise and Related Information" and has determined that it operates in one business segment dedicated to research in gene delivery technology.

#### RECENT ACCOUNTING PRONOUNCEMENTS

In December 1999, the SEC issued Staff Accounting Bulletin No. 101 - "Revenue Recognition" (SAB 101). SAB 101 reflects the SEC's views on revenue recognition. Historically the Company has recognized revenue from initial option and license fees in the period in which the agreement was signed if there were no significant performance obligations remaining. Revenue from milestone payments was recognized as revenue when the milestones were achieved. SAB 101 would require that revenue from option and license fees and milestone payments be deferred and recognized over the period of the option or license agreement. Companies which have not adhered to the guidance in SAB 101 will be required to reflect a cumulative effect adjustment of a change in accounting principle in their financial statements for the first fiscal quarter of the fiscal year beginning after December 15, 1999. The Company has not completed its evaluation of the impact of SAB 101 on its financial statements, however, the potential impact is expected to be material to the financial statements.

In June 1998, the FASB issued SFAS No. 133, "Accounting for Derivative Instruments and Hedging Activities." This statement changes the previous accounting definition of derivative, expanding it to include embedded derivatives and many commodity contracts. Under the Statement, every derivative is recorded in the balance sheet at its fair value, and any changes in the derivative's fair value are recognized currently in earnings unless specific hedge accounting criteria are met. SFAS No. 133 is effective for fiscal years beginning after June 15, 2000. The Company does not anticipate that the adoption of SFAS 133 will have a material impact on its financial position or results of operations.

#### 2. CASH EQUIVALENTS AND MARKETABLE SECURITIES

The Company invests its excess cash in debt instruments of financial institutions, corporations with strong credit ratings, and in U.S. government obligations. The Company has established guidelines relative to diversification

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and maturities that maintain safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates. Cash equivalents are short-term, highly liquid investments with original maturities of less than three months. Cash equivalents at December 31, 1999 and 1998, consist primarily of \$8,520,283 and \$11,671,743, respectively, in commercial paper, federal agency discount notes and money market funds.

In accordance with Statement of Financial Accounting Standards No. 115 ("SFAS 115"), "Accounting for Certain Investments in Debt and Equity Securities," the Company classifies its marketable securities as available-for-sale and records the unrealized holding gains or losses as a separate component of stockholders' equity. Realized gains or losses, calculated based on the specific identification method, were not material for the years ended December 31, 1999, 1998 and 1997.

At December 31, 1999, marketable securities consisted of the following:

<TABLE>  
<CAPTION>

	Amortized Cost	Market Value	Unrealized Loss
<S>	<C>	<C>	<C>
U.S. Government obligations	\$ 6,787,024	\$ 6,742,952	\$ (44,072)
Corporate bonds	17,835,525	17,747,168	(88,357)
Asset backed securities	2,043,433	2,035,061	(8,372)
	-----	-----	-----
Total marketable securities	\$26,665,982	\$26,525,181	\$ (140,801)
	=====	=====	=====

</TABLE>

Approximately 75 percent and 25 percent of these securities mature within one and two years, respectively, of December 31, 1999.

At December 31, 1998, marketable securities consisted of the following:

<TABLE>  
<CAPTION>

	Amortized Cost	Market Value	Unrealized Gain
<S>	<C>	<C>	<C>
U.S. Government obligations	\$ 5,508,897	\$ 5,529,915	\$ 21,018
Corporate bonds	17,051,442	17,086,242	34,800
Asset backed securities	3,986,160	3,999,782	13,622
<b>Total Marketable Securities</b>	<b>\$26,546,499</b>	<b>\$26,615,939</b>	<b>\$ 69,440</b>

</TABLE>

### 3. SIGNIFICANT CONTRACTS AND LICENSE AGREEMENTS

#### MERCK & CO., INC.

The Company has entered into three separate agreements with Merck & Co., Inc. ("Merck") which provide Merck with certain exclusive rights to develop and commercialize vaccines using the Company's "naked" DNA technology for certain disease targets. The 1991 and 1997 agreements are for human vaccine targets and the 1992 agreement is for animal vaccine targets. Prior to 1996, Merck exercised its options to seven preventive human infectious disease vaccines using the Company's naked DNA technology pursuant to the 1991 agreement. In November 1997, the Company and Merck amended the 1991 agreement and granted Merck certain rights to develop and market therapeutic vaccines against the human immunodeficiency virus (HIV) and hepatitis B virus (HBV). Under the amended agreement, Merck made an investment of \$5,000,000 for approximately 262,000 shares of the Company's common stock including a 25 percent premium over the average per share closing price for the twenty trading days prior to the date of the agreement. The premium of \$1,000,000 on the investment was reflected in revenue in 1997 and the balance of the investment, net of costs to issue the shares of stock, was reflected in common stock and additional paid-in capital. The September 1997 agreement between the Company and Merck granted Merck the rights to use the Company's naked DNA technology to deliver certain growth factors as potential treatments for a range of applications including revascularization. The agreement resulted in a payment to the Company of \$2,000,000.

In November 1999, Merck paid Vical \$2.0 million to extend an agreement covering therapeutic naked DNA vaccines. In December 1999, Merck started a Phase I clinical trial of a preventive naked DNA vaccine to protect against HIV infection. This event triggered a milestone payment of \$1.0 million which we received in January 2000. Vical accrued the revenue for this milestone in December 1999. Through December 31, 1999, the Company had

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received a total of \$21,130,000 (including the payment for the investment for common stock) under these agreements. License revenue recognized under these agreements was \$3,000,000, \$0, and \$3,000,000, in 1999, 1998, and 1997, respectively. All three agreements provide for the Company to receive additional payments based upon achievement of certain defined milestones and royalty payments based on net product sales.

#### PFIZER INC.

In January 1999, Pfizer Inc. entered into a collaborative and option agreement and a stock purchase agreement with the Company. Under the terms of the collaborative and option agreement, Pfizer Inc. paid the Company \$1,000,000 in option fees. In addition the Company agreed to provide access to two full time equivalent employees to assist Pfizer in its research and development efforts for \$500,000 of research and development expenses annually for three years. Under the terms of the stock purchase agreement Pfizer paid \$6,000,000 for the purchase of approximately 318,000 shares of common stock at \$18.87 per share, reflecting a 25 percent premium. The \$1,000,000 option fee and the \$1,200,000 premium on the purchase of stock were recognized as revenue in 1999, and the balance of the common stock investment, net of costs to issue the shares of stock, was reflected in common stock and additional paid-in capital in 1999. In 1999, the Company also recognized \$353,000 of revenue for research and development work.

#### MERIAL

The Company entered into a corporate alliance in March 1995 relating to DNA vaccines in the animal health area with Merial, a joint venture between Merck and Rhone Merieux. Merial has options to acquire exclusive licenses to our gene delivery technologies to develop and commercialize DNA-based vaccines to prevent infectious diseases in domesticated animals. Merial made payments of \$1,100,000 in 1999, and \$1,000,000 in 1998 to extend the options under this agreement. In December 1999, Merial paid the Company \$1.6 million for the initial exercise of options and extension of options under the agreement. License revenue recognized under this agreement was \$2,075,000, \$850,000 and \$500,000 in 1999, 1998 and 1997, respectively. If Merial exercises additional license options and markets these vaccines, cash payments and royalties on sales would be due to the Company.

#### AVENTIS PASTEUR (FORMERLY PASTEUR MERIEUX CONNAUGHT)

In September 1994, the Company entered into an agreement with Aventis Pasteur ("AP") that included a research collaboration and options for AP to take exclusive licenses to Vical's naked DNA vaccine technology for each of five vaccine targets. In addition, Vical was paid an annual research fee through September 1997 by AP for expenses incurred in performing certain preclinical work as defined in the agreement. Through 1996, AP had added another option and exercised four options. In 1997, AP paid the Company \$1,000,000 as a milestone payment under the agreement because the Company and AP began a Phase I clinical trial of an experimental vaccine against the parasite that causes malaria. The Company and AP sponsored the trial which was conducted by the U.S. Naval Medical Research Institute and the U.S. Army Medical Research Institute of Infectious Diseases. Through December 31, 1999, Vical has received \$7,816,000 of which \$0, \$239,000, and \$2,399,000 was recognized as revenue in 1999, 1998, and 1997, respectively. The agreement provides for the Company to receive additional payments based upon achievement of certain defined milestones and royalty payments based on net product sales.

**AVENTIS PHARMA (FORMERLY RHONE-POULENC RORER PHARMACEUTICALS, INC.)**

In October 1997, the Company and Aventis Pharma entered into an agreement granting Aventis Pharma an exclusive worldwide license to use the Company's naked DNA gene delivery technology to develop certain gene therapy products for potential treatment of neurodegenerative diseases. Under the terms of the agreement, the Company received \$1,000,000 which was recognized as revenue in 1997. This agreement provides for the Company to receive additional payments based upon achievement of certain defined milestones and royalty payments based on net product sales.

**CENTOCOR, INC.**

In February 1998, the Company signed an agreement allowing Centocor, Inc. ("Centocor") to use Vical's naked DNA technology to develop and market gene-based vaccines for the potential treatment of certain types of cancer. The agreement resulted in a payment to Vical of \$2,200,000, which was recognized as revenue in 1998. The payment represented an initial payment of \$2,000,000 under the license agreement and reimbursement of \$200,000 of patent costs. The Company may receive further payments plus royalties if Centocor successfully develops products using the Vical technology. The agreement grants to Centocor exclusive worldwide licenses and options to license Vical's naked DNA technology to deliver certain antigens to induce immune responses against the associated cancer cells.

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**BOSTON SCIENTIFIC CORPORATION**

In September 1998, the Company and Boston Scientific Corporation entered into a license and option agreement for the development of catheter-based intravascular gene delivery technology. The Company received \$1,100,000 which was recognized as revenue in 1998. The agreement also provides for the Company to receive royalty payments on net product sales.

**NAVAL MEDICAL RESEARCH INSTITUTE**

In September 1998, the Company signed a cooperative agreement with the Office of Naval Research to develop a multi-gene malaria DNA vaccine and test its ability to protect humans against malaria. This agreement, as amended, would provide up to \$2,813,000 of funding to Vical, of which \$1,778,000 and \$499,000 of contract revenue was recognized under this agreement in 1999 and 1998, respectively.

**OTHER RESEARCH AND LICENSING AGREEMENTS**

The Company also received revenue under research and licensing agreements with other entities including the U.S. government of which approximately \$1,296,000, \$933,000, and \$904,000, was recognized as revenue during the years ended December 31, 1999, 1998, and 1997, respectively.

Under the Merck, Aventis Pasteur, Merial, Aventis Pharma, Centocor, Pfizer, Human Genome Sciences, Inc. and Vascular Genetics Inc. (see Note 10 subsequent events) agreements, if the Company were to receive milestone or royalty payments, we would be required to pay up to 10 percent of some of these payments to Wisconsin Alumni Research Foundation. Under the Boston Scientific agreement, if the Company were to receive milestone or royalty payments, we would be required to pay up to 25 percent of some of these payments to the University of Michigan.

**4. OTHER FINANCIAL DATA**

Accounts payable and accrued expenses consisted of the following at December 31, 1999 and 1998:

<TABLE>  
<CAPTION>

	----- 1999 -----	----- 1998 -----
<S>	<C>	<C>
Accrued clinical trials cost	\$1,411,277	\$ 492,914
Employee compensation	880,797	692,716
Accounts payable	214,925	768,796

Accrued royalties payable	547,500	137,500
Other accrued liabilities	785,143	189,326
	-----	-----
	\$3,839,642	\$2,281,252
	=====	=====

</TABLE>

5. COMMITMENTS

LEASES

The Company leases its office and research facilities and certain equipment under operating and capital leases. The minimum annual rents on the office and research facilities are subject to increases based on changes in the Consumer Price Index subject to certain minimum and maximum annual increases. The Company is also required to pay taxes, insurance and operating costs under the facilities leases. Two of the three facilities leases can be renewed for one additional five year period beyond their expiration in 2004 and one facility lease can be renewed for two additional five-year periods. The equipment capital leases are secured by substantially all equipment of the Company.

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<TABLE>  
<CAPTION>

	Operating Leases	Capital Leases
	-----	-----
<S>	<C>	<C>
Years ending December 31,		
2000	\$1,339,586	\$ 721,398
2001	1,384,396	369,697
2002	1,430,744	267,812
2003	1,478,687	183,929
2004	1,394,788	-
2005	-	-
	-----	-----
Total minimum lease Payments	\$7,028,201	1,542,836
	=====	
Less amount representing Interest		(174,994)
		-----
Present value of capital lease payments		1,367,842
Less current portion		(627,957)
		-----
Long-term obligations under capital leases		\$ 739,885
		=====

</TABLE>

Rent expense for the years ended December 31, 1999, 1998, and 1997, was \$1,085,183, \$998,195, and \$969,899, respectively.

Cost and accumulated depreciation of equipment under capital leases were as follows:

<TABLE>  
<CAPTION>

	Cost	Accumulated Depreciation	Net
	-----	-----	-----
<S>	<C>	<C>	<C>
December 31, 1999	\$2,583,485	\$1,490,376	\$1,093,109
December 31, 1998	\$2,163,877	\$1,109,781	\$1,054,096

</TABLE>

NOTES PAYABLE

In November 1999, Vical entered into an unsecured line of credit agreement with a bank to provide financing for leasehold improvements. Under the terms of the agreement, Vical may borrow up to \$1,000,000 through May 1, 2000. Interest is payable monthly for any borrowings beginning November 1, 1999. Commencing June 1, 2000, the outstanding principal and interest will be repaid in 42 equal monthly payments. Interest under this agreement is at the bank's reference rate minus 0.25 percentage points. The borrowings can be prepaid without penalty. The agreement contains certain financial covenants. No borrowings were outstanding at December 31, 1999 under this agreement.

The Company also has a term loan which has an outstanding balance of \$106,887 and which bears interest at 9% at December 31, 1999. This loan will be paid by April 1, 2000.



RESEARCH AND LICENSE AGREEMENTS

In 1999 and 1998, the Company continued research and exclusive license agreements with various universities for continuing research and license rights to technology related to gene therapy. The agreements generally grant the Company the right to commercialize any product derived from specified technology. Fees paid are expensed as incurred and future obligations on these agreements are not significant.

6. STOCKHOLDERS' EQUITY

PREFERRED STOCK

The Company's certificate of incorporation, as amended, authorizes the issuance of up to 5,000,000 preferred shares. No shares of preferred stock were outstanding at December 31, 1999 or 1998.

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COMMON STOCK

The Company's certificate of incorporation, as amended, authorizes the issuance of up to 40,000,000 common shares. Common stock shares totaling 16,201,136 and 15,866,544 were outstanding at December 31, 1999 and 1998, respectively. (See Note 10--Subsequent Events-for discussion of stock offering completed in January 2000.)

STOCK PLAN AND DIRECTORS OPTION PLAN

The Company has a stock plan ("Stock Incentive Plan of Vical Incorporated") under which 3,200,000 shares of common stock are reserved for issuance to employees, non-employee directors and consultants of the Company. The plan provides for the grant of incentive and nonstatutory stock options and the direct award or sale of shares. The exercise price of stock options must equal at least the fair market value on the date of grant. The maximum term of options granted under the plan is ten years. Except for annual grants to directors which vest at the next annual meeting, options generally vest 25 percent on the first anniversary of the date of grant, with the balance vesting quarterly over the remaining three years. The plan has also limited the number of options that may be granted to any plan participant in a single calendar year to 300,000 shares.

The Company also has a directors stock option plan ("Directors Plan") that provides for the issuance to non-employee directors of up to 210,000 shares of the Company's common stock, of which options for 202,500 shares have been granted. The initial grant to a director of options under this plan generally vests 25 percent on the first anniversary of the date of grant, with the balance vesting quarterly over the remaining three years. In 1997, the stockholders approved an amendment to the Stock Incentive Plan of Vical Incorporated allowing non-employee directors to receive grants under that plan and, accordingly, it is not anticipated that there will be any future grants under the Directors Plan.

The following table summarizes stock option transactions for the Company's stock option plans for the years ended December 31, 1999, 1998 and 1997:

<TABLE>  
<CAPTION>

<S>	Shares <C>	Weighted Avg. Exercise Price <C>	Weighted Avg. Fair Value of Grants <C>
Outstanding, December 31, 1996	1,159,681	\$10.92	
Granted	403,845	\$14.14	\$10.17
Exercised	(72,922)	\$ 5.10	
Forfeited	(48,106)	\$13.25	
-----			
Outstanding, December 31, 1997	1,442,498	\$12.04	
Granted	580,875	\$15.56	\$11.12
Exercised	(135,228)	\$ 7.88	
Forfeited	(73,100)	\$13.99	
-----			
Outstanding, December 31, 1998	1,815,045	\$13.39	
Granted	546,900	\$17.89	\$13.06
Exercised	(16,623)	\$10.23	
Forfeited	(50,057)	\$15.19	
-----			
Outstanding December 31, 1999	2,295,265	\$14.45	

</TABLE>

The following table summarizes information about stock options outstanding under the Company's stock option plans at December 31, 1999:

<TABLE>  
<CAPTION>

Options Outstanding				Options Exercisable	
Range of Exercise Prices	Number Outstanding As of 12/31/99	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number Exercisable As of 12/31/99	Weighted Average Exercise Price
<S>	<C>	<C>	<C>	<C>	<C>
\$0.1600 - \$13.50 \$8.47	680,647	5.7	\$9.23	521,016	
\$13.63 - \$15.25 \$14.64	666,162	7.7	\$14.60	376,282	
\$15.38 - \$20.50 \$17.09	600,256	8.2	\$16.54	322,541	
\$20.75 - \$21.69 -	348,200	9.9	\$20.77	0	
\$0.1600 - \$21.69 \$12.65	2,295,265	7.6	\$14.45	1,219,839	

The number of shares and weighted average price of options exercisable at December 31, 1999, 1998 and 1997 were 1,219,839 shares at \$12.65, 844,829 shares at \$11.53, and 688,126 shares at \$9.90, respectively.

The Company has adopted the disclosure-only provisions of SFAS 123. Accordingly, no compensation cost has been recognized for the stock option plans. Had compensation cost for the Company's stock option plans been determined consistent with the provisions of SFAS 123, the Company's net loss and loss per share would have increased to the pro forma amounts indicated below:

<TABLE>  
<CAPTION>

	1999	1998	1997
<S>	<C>	<C>	<C>
Net loss - as reported	\$ 6,909,217	\$ 7,480,507	\$5,611,231
Net loss - pro forma	\$ 11,591,993	\$ 11,645,607	\$8,878,712
Net loss per share - as reported	\$ (0.43)	\$ (0.47)	\$ (0.36)
Net loss per share - pro forma	\$ (0.72)	\$ (0.74)	\$ (0.57)

</TABLE>

The fair value of each option grant was estimated on the date of grant using the Black-Scholes option-pricing model with the following weighted average assumptions used for grants: risk free interest rates of 5.70% (1999), 5.09% (1998), and 5.99% (1997) and, expected volatility of 71% (1999 and 1998), and 70% (1997). An expected option life of 5 years and a dividend rate of zero is assumed for all years presented.

#### 7. RELATED PARTIES

Included in other assets at December 31, 1999 and 1998, is the long-term portion of notes receivable, representing amounts due from certain officers and employees of the Company. Imputed interest is applied at the applicable federal rate. The loan agreements allow for the notes to be forgiven under certain circumstances over the next three years. The long-term portion is \$70,000 and \$60,000 at December 31, 1999 and 1998, respectively. The current portion, included in receivables and other, is \$50,000 and \$55,000 at December 31, 1999 and 1998, respectively.

#### 8. INCOME TAXES

As of December 31, 1999, the Company has available net operating loss carryforwards of approximately \$43,770,000 and research and development credit carryforwards of approximately \$3,400,000 to reduce future federal income taxes, if any. These carryforwards expire through 2019 and are subject to review and possible adjustment by the Internal Revenue Service.

Effective September 30, 1999, one of the Company's product candidates,

ALLOVECTIN-7 was granted orphan drug designation for the treatment of invasive and metastatic melanoma by the U.S. Food and Drug Administration (FDA) Office of Orphan Products Development. Orphan drug designation provides certain tax benefits for qualifying expenses.

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The Tax Reform Act of 1986 limits a company's ability to utilize certain net operating loss and tax carryforwards in the event of cumulative change in ownership in excess of 50 percent, as defined. The Company has completed numerous financings that have resulted in a change in ownership in excess of 50 percent, as defined. The utilization of net operating loss and tax credit carryforwards may be limited due to these ownership changes.

The Company has a deferred tax asset of approximately \$21,031,000 related primarily to its net operating loss and tax credit carryforwards. A valuation allowance has been recognized to offset the entire amount of the deferred tax asset as realization of such asset is uncertain.

9. EMPLOYEE BENEFIT PLANS

The Company has a net defined contribution savings plan under section 401(k) of the Internal Revenue Code. The plan covers substantially all employees. The Company matches employee contributions made to the plan according to a specified formula. The Company's matching contributions totaled approximately \$107,000, \$95,000, and \$94,000, in 1999, 1998, and 1997, respectively.

10. SUBSEQUENT EVENTS

On January 20, 2000, Vical completed a public offering of 3,450,000 shares of its common stock, including 450,000 shares issued to cover over-allotments, at a price of \$36.50 per share. Proceeds to Vical net of underwriting fees and offering expenses were approximately \$117,500,000.

On February 24, 2000, the Company and Human Genome Sciences, Inc. (HGS) signed a reciprocal royalty-bearing license. Under the agreement, Vical has the option to exclusively license up to three genes from HGS for gene-based product development. HGS has the option to license Vical's naked DNA gene delivery technology for use in up to three gene-based products. In addition, the Company granted an exclusive, royalty-bearing license to Vascular Genetics Inc. (VGI), a company in which HGS is a major shareholder, for naked DNA delivery of a gene with potential use for revascularization. In exchange, Vical received a minority equity interest in VGI.

11. SUMMARY OF UNAUDITED QUARTERLY FINANCIAL INFORMATION

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 1999 and 1998 (in thousands, except per share amounts):

<TABLE>  
<CAPTION>

	Quarter Ended			
	March 31	June 30	September 30	December 31
<S> 1999	<C>	<C>	<C>	<C>
Revenues 4,948	\$ 3,281	\$ 1,253	\$ 1,229	\$
Research and development costs 4,478	3,614	3,738	3,514	
Total operating expenses 5,652	4,627	4,860	4,581	
Net loss (195)	(809)	(3,068)	(2,837)	
Net loss per common share (basic and diluted) (0.01)	(0.05)	(0.19)	(0.18)	
Shares used in per share calculation 16,200	15,953	16,191	16,196	
<CAPTION>				
	March 31	June 30	September 30	December 31
<S> 1998	<C>	<C>	<C>	<C>
Revenues 932	\$ 2,732	\$ 560	\$ 1,696	\$

Research and development costs	3,095	3,058	3,158
2,743			
Total operating expenses	4,062	4,072	4,012
3,558			
Net loss	(721)	(2,935)	(1,750)
(2,075)			
Net loss per common share (basic and diluted)	(0.05)	(0.19)	(0.11)
(0.13)			
Shares used in per share calculation	15,753	15,789	15,817
15,892			

</TABLE>

CONSENT OF INDEPENDENT PUBLIC ACCOUNTANTS

As independent public accountants, we hereby consent to the incorporation of our report included in this Form 10-K into Vical Incorporated's previously filed Registration Statements Files No. 33-60826, No. 33-60824, No. 33-81602, No. 33-81600, No. 33-87972, No. 333-30181 and No. 333-80681.

ARTHUR ANDERSEN LLP

San Diego, California  
March 22, 2000

<TABLE> <S> <C>

<ARTICLE> 5

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THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE BALANCE SHEETS AND STATEMENTS OF OPERATIONS OF THE COMPANY'S FORM 10-K FOR THE YEAR ENDED DECEMBER 31, 1999, AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.

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