## SECURITIES AND EXCHANGE COMMISSION

# **FORM 10-K**

Annual report pursuant to section 13 and 15(d)

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## **FILER**

## MATRIX PHARMACEUTICAL INC/DE

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# UNITED STATES SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 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, 1998

OF

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

Commission File number: 0-19750

MATRIX PHARMACEUTICAL, INC.

(Exact name of registrant as specified in its charter)

DELAWARE 94-2957068

(State or other jurisdiction of

(I.R.S. Employer Identification No.)

incorporation or organization)

34700 CAMPUS DRIVE, FREMONT, CALIFORNIA (Address of principal executive offices)

94555 (Zip Code)

Registrant's telephone number, including area code: (510) 742-9900

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

TITLE OF EACH CLASS

NAME OF EACH EXCHANGE ON WHICH REGISTERED

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ON WHICH REGISTERED

ne N

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

COMMON STOCK, \$.01 PAR VALUE

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

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 Form 10-K or any amendment to this Form 10-K.

The aggregate market value of voting stock, \$.01 par value, held by non-affiliates of the registrant as of February 28, 1999: \$35,383,232.

Number of shares of Common Stock, \$.01 par value, outstanding as of February 28,1999: 22,278,942.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the following document are incorporated by reference into Part III of this Form 10-K Report: the Proxy Statement for the Registrant's 1999 Annual Meeting of Stockholders scheduled to be held on May 4, 1999.

MATRIX PHARMACEUTICAL, INC. FORM 10-K
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### PART I

## ITEM 1. BUSINESS

THIS FORM 10-K MAY CONTAIN, IN ADDITION TO HISTORICAL INFORMATION, FORWARD-LOOKING STATEMENTS THAT INVOLVE RISKS AND UNCERTAINTIES. THE COMPANY'S ACTUAL RESULTS COULD DIFFER MATERIALLY FROM THE RESULTS DISCUSSED IN ANY SUCH FORWARD-LOOKING STATEMENTS. FACTORS THAT COULD CAUSE OR CONTRIBUTE TO SUCH DIFFERENCES INCLUDE THOSE DISCUSSED IN "RISK FACTORS" AS WELL AS THOSE DISCUSSED ELSEWHERE IN THIS FORM 10-K.

## OVERVIEW

Matrix Pharmaceutical, Inc. ("Matrix" or "the Company") is a development-stage company that is developing novel drug product candidates for cancer based on its internal research and development capabilities and through licensing of product candidates from other pharmaceutical companies.

The Company is a leader in the formulation and development of novel pharmaceutical product candidates that are designed to improve the delivery of cancer drugs for more effective local treatment for solid tumors. The Company has applied its expertise in tumor biology and physiology, advanced imaging techniques, pharmaceutical chemistry, polymer chemistry, analytical chemistry and biochemistry, and chemical engineering to develop proprietary systems that facilitate the direct delivery and retention of anticancer agents in solid tumors. The Company has developed aqueous-based protein gel systems for delivery of water-soluble chemotherapeutic agents and non-aqueous semi-solid systems for delivery of chemotherapeutic agents that are poorly water soluble. Two product candidates that utilize the Company's aqueous-based protein gel systems are currently being evaluated in human clinical trials. These are IntraDose(TM) (cisplatin/epinephrine) Injectable Gel and MPI 5020 Radiopotentiator. IntraDose incorporates cisplatin, an established chemotherapeutic agent. MPI 5020 incorporates fluorouracil, another established chemotherapeutic agent.

In addition to developing product candidates based on its technology, the Company also licenses product candidates for development, utilizing its expertise to identify and subsequently implement appropriate development strategies for in-licensed compounds. In 1998, Matrix in-licensed FMdC, a systemic anticancer agent which has completed Phase I clinical trials. The Company is developing FMdC as an intravenously-administered therapeutic in non-small cell lung cancer and other cancers.

AQUEOUS-BASED PROTEIN SYSTEMS. IntraDose and MPI 5020 Radiopotentiator are based on the Company's patented injectable gel technology, in which a chemotherapeutic drug is combined with a protein matrix and, in IntraDose, a vasoconstrictor, to create an injectable gel. This gel enables targeted delivery of water-soluble drugs by direct injection into solid tumors and skin lesions. The Matrix delivery system localizes the release of drug, maintaining high drug concentrations at the tumor or lesion site and increasing the duration of exposure of the targeted tissue to the therapeutic agent. In IntraDose the activity of the drug can be further enhanced by the addition of epinephrine, a vasoconstrictor which reduces local blood flow and acts as a "chemical tourniquet" to hold the drug in place.

The Company believes that its technology may allow the development of new products from established drugs or agents which may be available from other companies or institutions. Whether or not the chosen drugs or compounds are "off-patent," when they are incorporated into the Company's proprietary drug delivery system, the resulting products are proprietary to the Company. The Company, therefore, expects to be competitive in the marketplace and have a proprietary position in such products for the length of the patents on its technology and resulting products.

Fluorouracil and cisplatin are widely used as systemic agents to treat solid tumors. These chemotherapeutic drugs exert a cytotoxic effect on dividing cells at various stages during their growth and multiplication. Cells that undergo rapid and unregulated cell division are more susceptible than normal cells to the effects of such drugs. Unfortunately, normal cells (E.G., bone marrow and gastrointestinal mucosa cells) rapidly divide and are also sensitive to the cytotoxic drugs. This toxicity to normal tissue limits the maximum dosing permitted with systemically administered chemotherapeutic drugs and often results in a tolerated dose that is substantially lower than the dose necessary to kill all diseased tissue. Suboptimal dosing contributes to the emergence of drug resistance among remaining cancer cells, complicating further drug therapy.

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The Company believes that the principal advantages of its aqueous-based protein systems technology include:

- SUSTAINED HIGH CONCENTRATIONS OF DRUG AT THE TARGET SITE. By maintaining high, local drug concentrations in the target tissue, the systems increase the exposure of diseased tissue to the drug.
- LOWERED SYSTEMIC TOXICITY. Because the systems concentrate the drug at the disease site and limit the drug exposure to normal tissues, overall systemic toxicity is reduced compared to systemic chemotherapy.
- SITE SPECIFIC APPLICATION. Products are injected directly into the tumor. Any accessible lesion or solid tumor which can be seen, palpated, or visualized with established imaging techniques or accessed directly or by means of minimally invasive techniques can potentially be treated.
- APPLICABILITY TO A BROAD RANGE OF THERAPEUTIC COMPOUNDS. Many conventional drugs and novel biopharmaceuticals can be delivered using the aqueous-based protein systems. This may allow the Company to utilize new or approved drugs and other biological agents available from other companies or institutions, thus reducing the risk, cost and time involved in drug discovery.

ANHYDROUS DELIVERY VEHICLES ("ADV"). Approximately half of the anti-cancer drugs in use today, including paclitaxel, etoposide, and teniposide, are poorly soluble in water, posing difficulties for administration by conventional systemic routes such as intravenous ("IV") injection or infusion. The solubilizing agents employed in several of these drug products to prepare suitable IV solutions may add to toxicity. The Company's approach to cancer treatment by local delivery of chemotherapeutic agents may obviate many of these difficulties. The Company has developed a series of non-aqueous polymer delivery vehicles (anhydrous delivery vehicles, or ADVs) which in preclinical experiments significantly enhance the local efficacy of these drugs compared to the efficacy obtained when these drugs are delivered systemically using more conventional aqueous delivery systems. The Company believes that ADV carriers may be applicable to a large variety of water-insoluble drugs, with the potential to significantly improve the clinical utility of these agents. The Company believes that this technology may also lend itself well to water-soluble drugs that have limited stability when dissolved in aqueous media. Until such time as a corporate partner is identified and additional financial resources are provided, the Company does not intend to initiate clinical development of any product

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## PRODUCTS IN CLINICAL DEVELOPMENT

The following table summarizes the Company's products in clinical development, the primary indications for each product and the current development status.

<TABLE> <CAPTION>

PRODUCT/INDICATION	METHOD OF ADMINISTRATION	DEVELOPMENT STATUS (1)	COMMERCIAL RIGHTS (2)
<s> INTRADOSE</s>	<c> Local intratumoral injection</c>	<c></c>	<c></c>
Head & Neck Cancer		Phase III	Matrix
Other Solid Tumors		Completed Phase III	Matrix
Liver Cancer - Primary		Phase II	Matrix
Liver Cancer - Metastatic Colorectal Cancer		Phase II Phase II	Matrix
FMDC	Intravenous (IV)		
Non-Small Cell Lung Cancer		Phase II	Matrix
MPI 5020 RADIOPOTENTIATOR	Local intratumoral injection		
Recurrent breast cancer (chest wall metastases)		Phase I/II	Matrix

#### </TABLE>

- (1) The Company's product candidates are generally developed in the following stages: pre-clinical studies (preparing to file an Investigational New Drug ("IND") Application in the United States or a Clinical Trial Exemption ("CTX") in foreign countries); clinical trials (which may include Phases I, II, III and IV and variants or combinations of the foregoing); regulatory submission (New Drug Application ("NDA") or Market Authorization Application ("MAA")); and cleared for marketing. See "-- Government Regulation."
- (2) The Company has worldwide rights to all product candidates except FMdC, for which the Company has licensed worldwide rights except for Japan.

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## INTRADOSE INJECTABLE GEL

Matrix is developing IntraDose Injectable Gel for a variety of solid tumors. Ninety percent of cancer patients suffer from solid tumors (I.E., carcinomas and sarcomas). Approximately 70% of these patients have local disease with no evidence of metastatic disease at the time of diagnosis. Conventional therapies for cancer include surgery, radiation and systemic drug therapy. Despite continued advances in these treatments, they are limited by negative side effects, such as loss of normal body functions, weakness, loss of appetite and nausea, which are the result of the killing, altering or removing of normal cell tissue. Therefore, quality of life factors such as pain management and control of other tumor related symptoms become important, as do the potential to retard disease progression and possibly prolong survival.

The Company's IntraDose product candidate represents a new approach to the treatment of solid tumors. IntraDose is designed for direct injection into solid tumors, including primary, metastatic and recurrent tumors. Imaging techniques such as endoscopy, ultrasound, computerized tomography ("CT" scan)

and magnetic resonance imaging ("MRI" scan) have substantially increased the number of solid tumors potentially treatable by the Company's products. The Company believes IntraDose may be efficacious when used as a single agent as well as when used in combination with conventional treatment modalities. In addition, the Company believes that treatments with IntraDose may be given in any out-patient setting that is equipped to administer cytotoxic drugs, offering the potential for cost-effective treatment without in-patient hospitalization for surgery or prolonged chemotherapy.

## HEAD AND NECK CANCER/OTHER SOLID TUMORS

The Company is currently conducting two placebo-controlled Phase III clinical trials for head and neck cancer. Open-label Phase III trials in other solid tumors including recurrent chest wall metastases (from breast cancer, ovarian cancer and lung cancer), esophageal cancer, melanoma, and various other carcinomas have been completed. These tumors may be either primary, recurrent, or metastatic. The Company believes that these cancers are well suited to a direct injection with the Company's IntraDose product as they are either visible, palpable or easily accessible with an endoscope. The Company plans to utilize data from its trials in head and neck cancer and other solid tumors to support approval of the broadest possible label for IntraDose in the United States and Western Europe.

HEAD AND NECK CANCER MARKET. The Company estimates that approximately 41,000 new cases of head and neck cancer are diagnosed annually in the United States and 73,000 new cases are diagnosed annually in Western Europe, based on data from the American Cancer Society and The International Agency for Research on Cancer, a unit of the World Health Organization. The incidence (number of new cases per year) is highest in countries with high rates of cigarette smoking and consumption of alcoholic beverages. Cancers of the head and neck are predominately squamous cell carcinomas. Of these, approximately 60% are diagnosed as later stage disease which has spread beyond the site of origin, and 40% are diagnosed as early stage disease that is localized. Cancers of the head and neck are often difficult to treat effectively with conventional surgery and radiotherapy techniques. Tumor location can make surgical resection difficult or impossible due to proximity to vital body structures and/or cosmetic or functional considerations, while radiotherapy often damages surrounding healthy tissues. The use of systemic chemotherapy in the management of head and neck cancers has been limited by the difficulty of achieving adequate and lasting tumor responses without incurring unacceptable side effects. This has led to a continuing investigation of new chemotherapeutics and combinations of chemotherapy, radiation, and surgery. The most important limitation of the available therapies for head and neck cancer is the high recurrence rate, generally 50% or higher.

A standard course of chemotherapy for patients with head and neck cancer often requires hospitalization with daily intravenous infusion of chemotherapy. The majority of patients who receive chemotherapy will also require ancillary supportive treatments, such as intravenous fluids, antiemetics or growth factor support to control the toxic side effects of the chemotherapy. Clinical results suggest that the use of IntraDose may not require some or any of these supportive treatments.

OTHER SOLID TUMOR MARKET. Tumors that can be accessed and injected directly or by means of an endoscopic procedure or minimally invasive technique include chest wall metastases from primary breast cancer, tumors of the esophagus, and malignant melanomas of the skin. The Company believes that approximately 75,000 cases are diagnosed each year in the United States (comprised of approximately 25,000 cases of chest wall metastases from primary breast cancer, 12,000 cases of esophageal cancer, and 38,000 cases of malignant melanoma) and that approximately 71,000 cases are diagnosed each year in Western Europe (approximately 26,000 in chest wall metastases from primary breast cancer, 24,000 in esophageal cancer, and 21,000 in malignant melanoma), based on data from the American Cancer Society and The

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International Agency for Research on Cancer. Recurrent solid tumors of these types were evaluated in the Company's open-label Phase III trials. Metastatic tumors found in the chest wall and other locations are usually treated with systemic chemotherapy and radiotherapy. However, this approach often leads to the development of drug resistance or cumulative radiation toxicity. Currently there are few treatment options for recurrent tumors.

CLINICAL STUDIES. An open-label Phase I/II clinical trial for the treatment of head and neck cancer and other solid tumors was conducted in 45 patients with a total of 82 treated tumors. The study was published in Otolaryngology-Head and Neck Surgery, the journal of the American Academy of Otolaryngology-Head and Neck Surgery Foundation. Forty-one of the 45 patients had received radiotherapy or cancer drug therapy prior to being treated with IntraDose, factors which reduce the likelihood of a significant response to the future use of chemotherapy. In this trial, 39% (32 of 82) of all treated tumors exhibited a complete response (100% reduction in tumor volume) and 50% of all

treated tumors (41 of 82) exhibited a complete response or partial response (greater than 50% reduction in tumor volume). A response was defined as tumor reduction of any duration, rather than duration lasting at least 28 days, the standard clinical definition of a response, because some patients received systemic chemotherapy for treatment of disease progression in distant, untreated tumors shortly after being treated with IntraDose. Sixteen of the complete responses (19.5% of treated tumors) without other therapy could be followed for at least 28 days and had a lasting complete response without other therapy. The median duration of complete response was 125 days.

IntraDose achieved these response rates in these patients with advanced disease without causing a clinically unacceptable level of systemic toxicity. Dose-limiting toxicity was not observed in this trial, and the overall side effects were deemed to be moderate in severity when compared to standard chemotherapy regimens. In addition, these patients did not experience any of the principal side effects associated with the systemic use of cisplatin, including nephrotoxicity and ototoxicity.

In June 1995, the Company announced initiation of two Phase III trials for patients with head and neck cancer and two trials for patients with other solid tumors. The double-blind, placebo-controlled Phase III head and neck cancer trials were designed to enroll approximately 180 evaluable patients, 90 patients in the United States trial and 90 patients in the European trial. Entry of patients in the Phase III trials for other solid tumor trials is now complete. These two Phase III studies are open-label studies designed to include approximately 130 evaluable patients, 65 in the United States and 65 in Western Europe. Patients enrolled in the Phase III trials had advanced recurrent or refractory disease. The study endpoints are objective tumor responses (I.E., tumor shrinkage of at least 50%) and achievement of pre-selected treatment goals, such as prevention of obstruction of vital structures, prevention of breakthrough of the skin, pain control, wound care, improvement in ability to hear, see, and eat, and other palliative benefits.

In June 1998, the Company announced that 60% of the 180 patients planned for the head and neck studies had been enrolled. The Company also disclosed that, in consultation with the FDA, study entry criteria have been revised to exclude patients with neck tumors close to the carotid artery, who are susceptible to cerebral vascular events including strokes and other serious neurological adverse events. As of year-end 1998, approximately 75% of the target number of patients had been enrolled in the head and neck studies. The Company intends to complete or close enrollment during the fourth quarter of 1999. Assuming these studies are successfully completed, the Company anticipates using the data from these trials to support regulatory submissions in the United States and Western Europe.

In September 1998, the Company announced that the other solid tumor studies were fully enrolled with 127 patients. In November 1998, preliminary clinical results were presented on a subset of patients at the 16th annual Chemotherapy Foundation Symposium. Data were presented on 30 women with advanced breast cancer and 25 patients with malignant melanoma. For most patients, two or more tumors were treated, including one that was identified by the physician before the start of treatment as most troublesome, that is, the tumor that was most threatening or bothersome to the patient. Objective tumor response rates of 47% in the most troublesome breast tumors and 44% in the most troublesome malignant melanomas were reported. Among the breast tumors, five of the 14 responses were complete (100% reduction of tumor volume for at least 28 days) and nine were partial (50% or greater reduction of tumor volume for at least 28 days). Among the melanomas, four of the  $11\,$ responses were complete and seven were partial. Seven of the 11 melanoma responses were sustained until the patients went off study. The other four patients received additional therapies during study follow-up for melanoma not treated with IntraDose. In patients with recurrent breast cancer, 40% (12/30) achieved a patient benefit as assessed by the investigator and/or the patient against predetermined treatment goals. Fifty-seven of the patients (8/19) who had reduction in tumor volume also had a corresponding patient benefit. Of the patients with malignant melanoma, 36% (9/25) achieved a patient benefit and 45% (5/11) of the patients with a tumor response also achieve a benefit. The therapy was generally well

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tolerated with fewer than 20% of the patients experiencing the nausea and vomiting usually related to intravenous chemotherapy. The most commonly reported side effects were local tissue reactions including but not limited to necrosis, erythema (redness) and swelling at the treatment site and injection-related pain.

LIVER CANCER

Two types of tumors are commonly found in the liver -- primary hepatocellular cancer (the most common cancer arising from liver cells) and tumors originating in other tissues (most commonly from colorectal tissues) that have metastasized to the liver. Primary liver cancer is a significant

health problem worldwide and especially in the parts of the world where hepatitis is prevalent (E.G., Japan, Korea and Southeast Asia). The Company believes the incidence of primary liver cancer is approximately 20,000 in the United States and 20,000 in Western Europe and the incidence of hepatic metastases from colorectal cancers is approximately 44,000 and 82,000 in the United States and Western Europe, respectively, based on data available from the American Cancer Society and The International Agency for Research on Cancer.

When possible, surgery is often the first line treatment for both types of liver tumors. However, a majority of patients with liver tumors are inoperable due to tumor location, tumor size, and extent of disease. For unresectable liver cancer, treatments have included the use of systemic chemotherapy, radiotherapy, liver transplantation, cryotherapy, hepatic arterial infusion of chemotherapy and chemoembolization (blocking or draining a blood vessel while injecting chemotherapy), all of which are applicable to only a minority of patients and have had only limited beneficial results. Due to the limited availability and effectiveness of current therapies, the Company believes that fewer than 50% of all patients with liver cancer are treated

Matrix believes that IntraDose may have utility as a first line treatment for many patients with unresectable liver cancer from either primary or metastatic liver tumors. Clinical investigators treated patients with both forms of unresectable liver cancer in a Phase I/II clinical trial program. The investigators treated 28 patients who had 25 tumors evaluable for tumor necrosis (tumor destruction, estimated by CT scan). Ten of the 25 evaluable tumors exhibited at least 90% necrosis in response to IntraDose treatment. Patients were treated in an outpatient setting, with the treatment quided by either CT or ultrasound.

Patients treated in this study have not experienced the typical side effects associated with intravenous cisplatin, such as nephrotoxicity, neurologic changes or ototoxicity. In addition, in a pharmacokinetics study conducted in patients treated at the M.D. Anderson Cancer Center, less than five percent of the platinum levels anticipated from a standard intravenous dose of cisplatin were found in patient plasma after treatment with IntraDose. The majority of the IntraDose product was confined to the treated tumor. The type and severity of side effects were similar to those experienced by patients treated for liver cancer.

In 1997, the Company initiated two open-label Phase II trials for patients with liver cancer. A Phase II trial for patients with primary liver cancer is in progress at medical centers in the United States, Europe, and Hong Kong. A Phase II trial for patients with cancers metastatic to the liver from colorectal cancer is underway at medical centers in the United States and Europe. These trials are designed to evaluate tumor necrosis and tumor response (as measured by CT scan), time to tumor progression, pattern of disease progression, and patient survival.

In April 1998, the Company announced that the criteria had been met to proceed beyond the first phase of enrollment of 17 patients in each trial, the first phase of the study, to the anticipated total enrollment of 37 patients in each. This decision was based on observation of changes in tumor volume or tumor necrosis in at least four patients in each study.

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## MPI 5020 RADIOPOTENTIATOR

Radiation therapy remains a critical tool in the management of many types of solid tumors. However, radiation resistance, hypoxic tumor cells, and normal tissue sensitivity to radiation has limited the benefit of this therapy. Using its platform technologies, the Company has demonstrated in preclinical experiments that intratumoral delivery of radiopotentiating agents significantly enhances the effects of radiation in solid tumors. The Company's lead candidate in this area, MPI 5020, is a fluorouracil (5-FU)-based product that uses the Company's aqueous protein gel technology.

In 1997, the Company initiated a Phase I/II trial in chest wall metastatic disease from recurrent breast cancer at medical centers in the United States. This dose-escalation study is intended to evaluate the safety of MPI 5020 when administered in conjunction with standard radiotherapy and to compare the effect on tumor regression of tumors treated with MPI 5020 and radiotherapy to tumors treated with radiotherapy alone.

Preliminary information from this ongoing trial was reported at the annual meeting of the American Society for Therapeutic Radiation and Oncology in October 1998 and at the Annual San Antonio (Texas) Breast Cancer Symposium in December 1998. Patients have been treated in the first three of the six planned dose-escalation and frequency-schedule treatment regimens, and the

combined use of radiation therapy and MPI 5020 has been feasible and well

FMdC

FMdC is a new chemical entity that belongs to a class of anticancer and antiviral agents known as nucleoside analogs. Several nucleoside analogs are marketed for treatment of certain leukemias or lymphomas, malignancies of white blood cells. In addition, another nucleoside analog is marketed for treatment of pancreatic cancer and non-small cell lung cancer, both of which are solid tumor malignancies. Preclinical testing indicates that FMdC has activity against solid tumors and may also be active against blood cell cancers

FMdC is an analog of deoxycytidine, one of the four nucleotides, or bases, that form DNA. Researchers believe FMdC has several modes of action. The two most important of these are thought to be DNA chain termination during DNA replication and repair and inhibition of ribonucleotide reductase, an enzyme that manufactures nucleotides (nucleic acid bases) for incorporation into DNA. FMdC can be incorporated directly into the replicating strand of DNA. Once FMdC is incorporated, the enzymes responsible for further synthesis cannot add additional nucleotides to the DNA chain. This causes the DNA chain to terminate before it is completely copied and leads to the death of the cell. The incorporation of FMdC into DNA is also facilitated by FMdC's inhibition of ribonucleotide reductase, as this inhibition reduces the supply of the nucleic acid bases that are necessary for DNA replication. Additionally, experiments indicate that FMdC suppresses production of a protein that stimulates the growth of blood vessels near tumors, suggesting that FMdC also may have anti-angiogenic properties.

Animal studies indicate that FMdC is effective against a broad spectrum of human and rodent tumors, including tumors of the lung, colon, breast (estrogen-dependent and estrogen-independent), prostate, ovaries, and pancreas. It has been shown in laboratory studies to be a more effective DNA chain terminator and inhibitor of ribonucleotide reductase than certain other nucleoside analogs with known cytotoxic activity.

In an intravenous dosage form, FMdC was generally well tolerated in four Phase I studies conducted by Hoechst Marion Roussel, Inc. Side events included fever, flushing, and clinically manageable reductions in white blood cell counts. FMdC has a relatively long plasma half life of three to six hours, which also may make it more effective than other nucleoside analogs. A Phase I trial of an oral dosage form of FMdC has been completed by Kyowa Hakko, Ltd., which owns rights to the compound in Japan.

In February 1999, a Phase II study of FMdC in patients with non-small cell lung cancer was initiated in the United States. The American Cancer Society estimates that non-small cell lung cancer is the leading cause of cancer deaths in the United States, accounting for 75% of the 160,100 lung cancer deaths expected this year as well as 75% of the 171,500 expected new cases of lung cancer. Lung cancer is also one of the most common forms of cancer and one of the most frequent causes of death from cancer in the European Union. The International Agency for Research on Cancer estimates that 182,398 new cases of lung cancer are diagnosed each year in the European Union and 173,042 deaths occur each year from lung cancer. The Company expects to begin Phase II trials in one or more additional indications beyond non-small cell lung cancer during 1999.

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Non-small cell lung cancer is frequently initially treated with surgery or radiation treatments, although patients may not be eligible for surgery. Relapse rates are high due, it is believed, to the presence of metastatic disease. For relapsing patients, treatment options are single-agent chemotherapy, combination-agent chemotherapy, or best supportive care. The advent of newer chemotherapeutic agents (e.g. carboplatin, paclitaxel, docetaxel, vindesine, vinorelbine, irinotecan, topetecan, gemcitabine) has improved patient response, but durable complete responses for more than one year are infrequently achieved. Effective new agents with novel mechanisms of anticancer activity and favorable toxicity profiles are needed to improve the outcome for these patients.

## PRECLINICAL PROGRAMS

The Company has focused preclinical research efforts on delivery of topoisomerase inhibitors and tubulin-binding agents through Matrix's proprietary ADV technology. Topoisomerase inhibitors and tubulin-binding agents are classes of chemical compounds that have demonstrated potent anti-cancer activity IN VITRO and IN VIVO but are poorly water soluble. In order to be administered intravenously, many of these chemical compounds have been formulated with solubilizing agents that may cause serious systemic side effects. The Company believes its ADV technology may improve the therapeutic ratio (I.E., to increase a drug's local effectiveness and/or significantly reduce dose-limiting side

effects which result from its systemic administration) of these and other poorly water soluble anti-cancer agents.

Clinical development of the ADV technology will depend on the ability of the Company to secure funding from other pharmaceutical companies.

## ACCUSITE-TM- INJECTABLE GEL

AccuSite (fluorouracil/epinephrine) Injectable Gel, the first product developed by the Company, has been approved for treatment of genital warts in Belgium, Denmark, Germany, Ireland, Italy, Luxembourg, the Netherlands, and the United Kingdom. A regulatory decision is pending in France. However, in September 1997, the Company indefinitely suspended, both within the United States and other countries, further development and commercialization programs related to AccuSite after receiving a second action letter from the United States Food and Drug Administration ("FDA") with respect to the Company's application for U.S. marketing clearance of AccuSite. The FDA action letter reiterated concerns expressed by the agency in December 1996 about the safety profile of AccuSite and, in particular, about the persistence in certain AccuSite-treated patients of a bump-like thickening or swelling (induration) at the site of injection, which the agency believes could indicate an inflammatory process. In subsequent meetings, FDA officials have maintained this position and indicated that reconsideration of the Company's New Drug Application would require further clinical trials. The Company does not intend to conduct such studies or otherwise invest substantial Company resources in pursuit of marketing clearance in the United States. The Company has also concluded that in the absence of commercialization in the United States, it would not be cost effective to market AccuSite in Europe through local partners.

#### MANUFACTURING AND SUPPLY

Matrix maintains worldwide manufacturing rights to all of its products. The Company has manufactured AccuSite and IntraDose at facilities it has operated in San Jose and Milpitas, California, as well as at a contract manufacturing facility. The Company's San Jose and Milpitas facilities were closed during 1998 as part of a restructuring of the Company's work force and consolidation of manufacturing operations in a 67,000 square foot research and manufacturing facility in San Diego, California, which the Company acquired in 1995. Following extensive renovations, the San Diego facility became operational in 1998 for the aseptic processing of collagen gel, sterile filling operations and non-sterile processing of collagen gel, as well as for all materials-receiving activities, labeling, packaging and shipping operations. The Company intends to use the San Diego facility to meet its near-term clinical trials and long-term commercial scale production requirements for IntraDose and MPI 5020. The Company may also utilize the San Diego facility for contract manufacturing for other pharmaceutical companies in order to generate near-term revenues. The facility has passed inspection by the State of California but will require approval by the U.S. Food and Drug Administration prior to commercialization of products manufactured there. In March 1998, the Company entered into a sale and leaseback agreement for the San Diego facility. See Item 2, "Properties." FMdC will not be manufactured by the Company. The Company has acquired supplies of FMdC sufficient for anticipated near-term needs and intends to contract for longer-term production needs.

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The Company's ability to conduct clinical trials on a timely basis, to obtain regulatory approvals and to commercialize its products will depend in part upon its ability to manufacture its products, either directly or through third parties, at a competitive cost and in accordance with applicable FDA and other regulatory requirements, including cGMP regulations. Several of the materials used in the Company's products are available from a limited number of suppliers. These items, including collagen gel and bulk drug substance, have generally been available to Matrix and others in the pharmaceutical industry on commercially reasonable terms. If the Company's manufacturing facilities are not able to produce sufficient quantities of collagen gel in accordance with applicable regulations, the Company would have to obtain collagen gel from another source and gain regulatory approval for that source. Matrix has negotiated and intends to continue to negotiate supply agreements, as appropriate, for the raw materials and components utilized in its products.

## SALES AND MARKETING

The Company currently owns worldwide marketing rights for all its products under development, except for FMdC in Japan. The Company's business strategy is to market or co-market IntraDose and its other oncology product candidates, if approved, in the United States and to license its products outside the United States to pharmaceutical partners who have substantially greater resources and experience in local markets. See "Risk Factors - We Have

## PATENTS AND PROPRIETARY RIGHTS

The Company's policy is to aggressively seek patent protection and to enforce all of its intellectual property rights. In the United States, the Company has eight issued patents, three allowed patents, and four pending applications. In Western Europe, the Company has three issued patents and seven pending applications. The Company has three issued patents and several pending applications in Japan. Three of the five patents issued in the United States relate to the Company's base technologies. The first of these three patents claims compositions consisting of collagen or fibrinogen as protein matrices, cytotoxic and antiproliferative drugs, and (optionally) a vasoconstrictive agent. This patent expires in the United States in 2003 and also covers the method of use of these compositions in treating cancerous or hyperproliferative lesions by local application. The second patent, which expires in the United States in 2007, includes pharmaceutical compositions consisting of a range of cytotoxic agents (including radionuclides, etc.) in combination with vasoconstrictive agents and (optionally) a variety of other tissue modifiers, formulated in aqueous pharmacologically acceptable vehicles. The method of use of these compositions in treating cancerous lesions by local application is also covered. The third patent covers certain formulations of the ADV technology for delivering water-insoluble anti-cancer drugs, and specifically covers water-immiscible fatty acid ester matrices containing cytostatic agents and their use for treating cancer via intralesional administration. Another issued patent in the United States, which expires in 2015, covers certain drug-containing collagen gels, including AccuSite, MPI 5020 and, potentially, other products developed by the Company. The other allowed patents cover a key aspect of the Company's collagen manufacturing process

As part of the in-licensing agreement on FMdC, the Company has received licenses to a patent portfolio on this technology in the United States, Europe and many other countries with the exception of Japan. The first of these patent families is a composition-of-matter and method-of-use case covering FMdC (and related compounds) and their use in treating neoplastic or viral disease. The European patents in this family expire in 2009, and the last of the U.S. patents in this family expires in 2014. A second patent family covers the synthetic method by which FMdC is made; the last of these patents expire in 2013 in the United States and Europe. Another U.S. patent covers the use of combinations of FMdC and radiation (U.S. expiry 2014, ex-U.S. in prosecution) and several other synthetic process and method-of-use patents (combination chemotherapy with other cytotoxic drugs, combination antiviral therapy, etc.) are issued in Europe or in prosecution in the United States and Europe.

## COMPETITION

The development of therapeutic agents for human disease is intensely competitive. Many different approaches are being developed or have already been adopted for routine use for the management of diseases targeted by the Company. Certain cancers and skin diseases are targets for therapeutic product development at numerous entities, many of which have greater human and financial resources than the Company. In addition, conventional drug therapy, surgery and other more established treatments and modalities will compete with the Company's products.

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The pharmaceutical industry is subject to rapid and substantial technological change. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Most of these entities have significantly greater research and development capabilities, as well as substantial marketing, financial and managerial resources, and represent significant competition for the Company. Acquisitions of, or investments in, competing biotechnology companies by large pharmaceutical companies could increase such competitors' financial, marketing and other resources. There can be no assurance that developments by others will not render the Company's products or technologies noncompetitive, or that the Company will be able to keep pace with technological developments. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing the therapeutic effect than products being developed by the Company. These competing products may be more effective and less costly than the products developed by the Company.

The Company's competitive position depends upon, among other factors, its ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary products or processes and secure sufficient capital resources to complete product development and regulatory processes. The Company expects that competition among products approved for sale will be based,

among other factors, on product activity, safety, reliability, availability, price, patent position and new usage and purchasing patterns established by managed care and other group purchasing organizations.

## GOVERNMENT REGULATION

The Company and its products are subject to comprehensive regulation by the FDA in the United States and by comparable authorities in other countries. These national agencies and other federal, state, and local entities regulate, among other things, the preclinical and clinical testing, safety, effectiveness, approval, manufacture, labeling, marketing, export, storage, record keeping, advertising, and promotion of the Company's products.

The process required by the FDA before the Company's products may be approved for marketing in the United States generally involves (i) preclinical laboratory and animal tests; (ii) submission to the FDA of an IND, which must become effective before clinical trials may begin; (iii) adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for its intended indication; (iv) submission to the FDA of an NDA, and; (v) FDA review of the NDA in order to determine, among other things, whether the drug is safe and effective for its intended uses. When a product contains more than one active drug component, as do some of the Company's current product candidates, the FDA may request that additional data be submitted in order to demonstrate the contribution of each such component to clinical efficacy.

Clinical trials are typically conducted in three sequential phases which may overlap. During Phase I, when the drug is initially given to human subjects, the product is tested for safety, dosage tolerance, absorption, metabolism, distribution, and excretion. Phase II involves studies in a limited patient population to (i) evaluate preliminarily the efficacy of the product for specific, targeted indications, (ii) determine dosage tolerance and optimal dosage, and (iii) identify possible adverse effects and safety risks. Phase III trials are undertaken in order to further evaluate clinical efficacy and safety within an expanded patient population at geographically dispersed clinical study sites. The FDA may suspend clinical trials at any point in this process if it concludes that clinical subjects are being exposed to an unacceptable health risk.

FDA approval of the Company's products, including a review of the manufacturing processes and facilities used to produce such products, is required before such products may be marketed in the United States. The process of obtaining approvals from the FDA can be costly, time consuming, and subject to unanticipated delays. Any failure or delay in obtaining such approvals would adversely affect the ability of the Company to market its proposed products. Moreover, even if regulatory approval is granted, such approval may include significant limitations on indicated uses for which a product could be marketed.

The processes required by European regulatory authorities before the Company's products can be marketed in Western Europe are similar to those in the United States. First, appropriate preclinical laboratory and animal tests as well as analytical product quality tests must be done, followed by submission of a CTX or similar documentation before human clinical trials can be initiated. Upon completion of adequate and well controlled clinical trials in humans that establish the drug is safe and efficacious, regulatory approval must be obtained from the relevant regulatory authorities.

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The proposed products and technologies of the Company may also be subject to certain other federal, state, and local government laws and regulations, including, but not limited to, various environmental laws, the Occupational Safety and Health Act, and state, local, and foreign counterparts to such laws. Compliance with such laws and regulations does not have, nor is such compliance presently expected to have, a material adverse effect on the business of the Company.

## RESEARCH AND DEVELOPMENT

The Company's sponsored research and development expenses were approximately \$24,320,000, \$27,214,000 and \$21,589,000 in 1996, 1997, and 1998, respectively.

## EMPLOYEES

As of December 31, 1998, the Company had a total of 97 full-time employees, including 23 in research and development, 23 in medical and regulatory affairs, biostatistics, and technical services, 29 in manufacturing, and 22 in other departments. The Company believes that it has been successful in attracting skilled and experienced personnel; however, competition for such personnel is intense and there can be no assurance that the Company will be successful at attracting and retaining qualified personnel in the future. None of the Company's employees are covered by collective bargaining agreements and management considers relations with its employees to be good.

#### RISK FACTORS

## WE CAN GIVE NO ASSURANCE OF REGULATORY APPROVALS

The preclinical and clinical testing, manufacturing, and marketing of our products are subject to extensive regulation by numerous governmental authorities in the United States and other countries, including the Food and Drug Administration ("FDA"). Among other requirements, the FDA must approve our product candidates, manufacturing processes and production facilities before we may market them in the United States. Similarly, a foreign governmental authority must typically approve the marketing of a product before that product's manufacturer can market it in a particular foreign country. We have no products approved by the FDA and although AccuSite has been approved by foreign authorities, we do not expect to achieve profitable operations unless other product candidates now under development receive FDA and foreign regulatory approval and are thereafter commercialized successfully. We have had only limited experience in submitting and pursuing regulatory applications. The process of obtaining FDA approvals can be costly, time consuming and subject to unanticipated delays, and we can give no assurance that the FDA will grant us any approvals on a timely basis, or at all.

The process of obtaining FDA regulatory approval involves a number of steps that, taken together, may involve seven years or more from the initiation of clinical trials and require the expenditure of substantial resources. Among other requirements, this process requires that the product candidate undergo extensive preclinical and clinical testing to demonstrate its safety and efficacy for its intended uses. We must also file a New Drug Application ("NDA") requesting FDA approval. When a product contains more than one component that contributes to the product's effect, as do some of our current product candidates, the FDA may request that additional data be submitted in order to demonstrate the contribution of each such component to clinical efficacy.

In addition, prior to approval of a product, the FDA must inspect and accept the product's manufacturing facilities as being in compliance with its Good Manufacturing Practices ("GMP") regulations. We can give no assurance that the FDA will accept our San Diego manufacturing facility, and failure to receive or maintain such acceptance would materially and adversely affect our business.

When we submit an NDA, the FDA must review and interpret our analysis of the results of our clinical studies submitted as part of the NDA. Any FDA interpretation may differ from our analysis, and we can give no assurance that the FDA will accept our data or our interpretation of that data. In addition, changes in applicable law or FDA policy during the period of product development and FDA regulatory review may result in the delay or rejection of our NDA. Any failure to obtain, or delay in obtaining, FDA approvals would adversely affect our ability to market our proposed products. Moreover, even if FDA approval is granted, the approval may include significant limitations on indicated uses for which a product could be marketed.

Violations of regulatory requirements at any stage, including the preclinical and clinical testing process, the approval process or after approval, may result in adverse consequences, including the FDA's delay in approving or refusal to approve a product, withdrawal of an approved product from the market, and/or the imposition of criminal penalties against the manufacturer and/or the NDA holder. In addition, the subsequent discovery of previously unknown problems relating to a marketed product may result in restrictions on such product, manufacturer, or the NDA holder, including withdrawal of the product from the market. Also, new government requirements may be established that could delay or prevent regulatory approval of our products under development.

The processes required by European regulatory authorities before our product candidates can be marketed in Western Europe are similar to those in the United States. We must first complete appropriate preclinical laboratory and animal tests as well as analytical product quality tests and then submit a clinical trial exemption or similar documentation before we can initiate human clinical trials. Upon completion of adequate and well-controlled clinical trials in humans that establish that the drug is safe and efficacious, we must obtain regulatory approval from the relevant regulatory authorities.

## UNCERTAINTIES ASSOCIATED WITH CLINICAL TRIALS

We have conducted and plan to continue to undertake extensive and

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or the FDA may modify or suspend clinical trials at any time if the FDA concludes that the subjects or patients participating in the trials are being exposed to unacceptable health risks. Further, we can give no assurance that human clinical testing will show any current or future product candidate to be safe and effective or provide data suitable for submission to the FDA.

We are currently conducting multiple clinical trials in the United States and certain foreign countries, including two ongoing Phase III trials. The rate of completion of our clinical trials depends upon, among other factors, the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites and the eligibility criteria for the study. We have experienced slower than planned accrual of patients in our ongoing Phase III trials. Further delays in completing enrollment in these trials or delays in other clinical studies may result in increased costs and delays, which could materially and adversely affect our business. Generally, similar considerations apply to clinical testing that is subject to regulatory oversight by foreign authorities and/or that is intended to be used in connection with foreign marketing applications.

## WE HAVE A HISTORY OF LOSSES AND OUR FUTURE PROFITABILITY IS UNCERTAIN

We incorporated in 1985 and have experienced significant losses since that date. As of December 31, 1998, our accumulated deficit was approximately \$166,969,000. We have not generated revenues from our products or product candidates and expect to incur significant additional losses over the next several years. In order to achieve a profitable level of operations, we must successfully develop products, obtain regulatory approvals for our products, enter into agreements for product commercialization outside the United States, and develop an effective sales and marketing organization in the United States. We can give no assurance that we will complete our product development efforts, that we will obtain the required regulatory approvals, that we will manufacture or market any products successfully, or that we will achieve profitability.

### WE WILL REQUIRE ADDITIONAL FINANCING

We have expended and will continue to expend substantial funds to complete the research and development of our product candidates. We may require additional funds for these purposes through additional equity or debt financings, collaborative arrangements with corporate partners or from other sources. We can give no assurance that such additional funds will be available on acceptable terms, if at all. Our business could be materially and adversely affected if adequate funds are not available from operations or additional sources of financing. Based on our current operating plan, we anticipate that our existing capital resources will be adequate to satisfy our capital needs through 2000. See "Management's Discussion and Analysis of Financial Condition and Results of Operations."

## WE HAVE LIMITED MANUFACTURING AND SALES AND MARKETING EXPERIENCE

We intend to market and sell certain of our product candidates, if successfully developed and approved, through our own dedicated sales force in the United States and through pharmaceutical licensees in Europe. We can give no assurance that we will be able to establish a successful direct sales organization or co-promotion or distribution arrangements. In addition, we can give no assurance that resources will be available to us to fund our marketing and sales expenses, many of which must be incurred before sales commence. Failure to establish a marketing and sales capability in the United States and/or outside the United States may materially and adversely affect our

Our ability to conduct clinical trials on a timely basis, to obtain regulatory approvals and to commercialize our products will depend in part upon our ability to manufacture our products, either directly or through third parties, at a competitive cost and in accordance with applicable FDA and other regulatory requirements, including GMP regulations. We closed our manufacturing facilities in San Jose and Milpitas, California in March 1998 and transferred manufacturing personnel to a research and manufacturing facility in San Diego, California that we acquired in 1995 to meet our anticipated long-term commercial scale production requirements. We expect that the San Diego facility and contract manufacturers should provide sufficient production capacity to meet clinical requirements. We can give no assurance that we will be able to validate this facility in a timely manner or that this facility will be adequate for our long-term needs without delaying our ability to meet product demand or to manufacture in a cost-effective manner. We expect to continue to use selected contract

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#### WE DEPEND ON OUR SOURCES OF SUPPLY

Several of the materials used in our product candidates are available from a limited number of suppliers. These items, including collagen gel and various bulk drug substances, have generally been available to us and others in the pharmaceutical industry on commercially reasonable terms. If our manufacturing facilities are not able to produce sufficient quantities of collagen gel in accordance with applicable regulations, we would have to obtain collagen gel from another source and gain regulatory approval for that source. We can give no assurance that we would be able to locate an alternative, cost-effective source of supply of collagen gel.

We have negotiated and intend to continue to negotiate supply agreements, as appropriate, for the raw materials and components utilized in our products. Any interruption of supply could have a materially and adversely affect our ability to manufacture our products, complete clinical trials, or commercialize our products. In addition, the issuance in 1996 of a U.S. patent for cisplatin, a chemotherapeutic drug that is the active compound in our IntraDose Injectable Gel product, could limit our ability to commercialize this product in the United States if the newly-issued patent were upheld, if IntraDose were found to infringe that patent, and if we were unable to obtain a license under that patent. See "Uncertainty Regarding Patents and Proprietary Rights."

## UNCERTAINTY REGARDING PATENTS AND PROPRIETARY RIGHTS

Our success depends in part on our ability to obtain patent protection for our products and to preserve our trade secrets and operate without infringing on the proprietary rights of third parties. We have not conducted an exhaustive patent search and we can give no assurance that patents do not exist or could not be filed which would materially and adversely affect our ability to market our products or maintain our competitive position with respect to our products. Our patents may not prevent others from developing competitive products using related technology. Other companies that obtain patents claiming products or processes useful to us may bring infringement actions against us. As a result we may be required to obtain licenses from others to develop, manufacture or market our products. We can give no assurance that we will be able to obtain any such licenses on commercially reasonable terms, if at all. We also rely on trade secrets and proprietary know-how that we seek to protect, in part, by confidentiality agreements with our employees, consultants, suppliers and licensees. We can give no assurance that these third parties will not breach these agreements, that we would have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently developed by competitors.

We can give no assurance that the U.S. Patent and Trademark Office ("PTO") will approve our pending patent applications, that any patent issued to, or licensed by us will provide protection that has commercial significance. In this regard, the patent position of pharmaceutical compounds and compositions is particularly uncertain. Even issued patents may later be modified or revoked by the PTO in proceedings instituted by us or others. In addition, we can give no assurance that our patents will afford protection against competitors with similar compounds or technologies, that others will not obtain patents with claims similar to those covered by our patents or applications, or that others' patents will not adversely affect our ability to conduct our business.

In 1996, for instance, the PTO granted a composition-of-matter patent for the cytotoxic drug cisplatin in the United States to a pharmaceutical company whose use patent on cisplatin as an anti-tumor agent expired in December 1996. We believe, on advice of patent counsel, that our IntraDose product candidate, which contains cisplatin, does not infringe this patent and also that new patent may have been improperly awarded and should be found invalid and/or unenforceable. However, if the new patent on cisplatin is upheld and if IntraDose were found to infringe that patent, there can be no assurance that we would be able to obtain a license to the patent on commercially reasonable terms, if at all, in order to commercialize IntraDose in the United States.

We believe that obtaining foreign patents may be more difficult than obtaining domestic patents because of differences in patent laws, and recognize that our patent position therefore may be stronger in the United States than abroad. In addition, the protection provided by foreign patents, once they are obtained, may be weaker than that provided by domestic patents.

## RISKS RELATED TO RAPID TECHNOLOGICAL CHANGE AND SUBSTANTIAL COMPETITION

The pharmaceutical industry is subject to rapid and substantial technological change. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Most of these entities have significantly greater research and development capabilities, as well as substantially more marketing, financial and managerial resources than us, and represent significant competition for us. Acquisitions of, or investments in, competing biotechnology companies by large pharmaceutical companies could increase these competitors' financial, marketing and other resources. We can give no assurance that developments by others will not render our products or technologies noncompetitive or that we will be able to keep pace with technological developments. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing similar therapeutic effects than products that we are developing. These competing products may be more effective and less costly than the products that we are developing. In addition, conventional drug therapy, surgery and other more familiar treatments and modalities will compete with our products.

Any product that we successfully develop and for which we gain regulatory approval must then compete for market acceptance and market share. Accordingly, important competitive factors, in addition to completion of clinical testing and the receipt of regulatory approval, will include product efficacy, safety, timing and scope of regulatory approvals, availability of supply, marketing and sales capability, reimbursement coverage, pricing and patent protection.

## PHARMACEUTICAL PRICING AND ADEQUATE REIMBURSEMENT IS UNCERTAIN

The continuing efforts of governmental and third party payers to contain or reduce the costs of health care through various means may affect the future revenues, profitability, and availability of capital for biopharmaceutical companies. For example, in certain foreign markets pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar government control. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially and adversely affect our prospects.

Our ability to commercialize our products successfully will depend in part on the extent to which appropriate reimbursement levels for the cost of such products and related treatment are obtained from government authorities, private health insurers and other organizations, such as health maintenance organizations, or HMOs. Third-party payers are increasingly challenging the prices charged for medical products and services. Also, the trend towards managed health care in the United States and the concurrent growth of organizations like HMOs, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may limit prices we can charge for our products. The cost containment measures that health care payers and providers are instituting and the effect of any health care reform could adversely affect our ability to sell our products and may materially and adversely affect our business.

## WE DEPEND ON QUALIFIED AND KEY PERSONNEL

Because of the specialized nature of our business, our ability to maintain our competitive position depends on our ability to attract and retain qualified management and scientific personnel. Competition for such personnel is intense. We can give no assurance that we will be able to continue to attract or retain such persons.

## RISKS ASSOCIATED WITH PRODUCT LIABILITY EXPOSURE; LIMITED INSURANCE COVERAGE

We face an inherent business risk of exposure to product liability claims in the event that the use of products during research or commercialization results in adverse effects. While we will continue to take appropriate precautions, we can give no assurance that we will avoid significant product liability exposure. Although we maintain product liability insurance for clinical studies, we can give no assurance that this coverage will be adequate or that adequate insurance coverage for future clinical or commercial activities will be available at all, or at an acceptable cost, or that a product liability claim would not materially adversely affect our business or financial condition.

Our research and development involves the controlled use of hazardous materials, such as cytotoxic drugs, other toxic and carcinogenic chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by federal, state and local regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of this type of accident, we could be held liable for any resulting damages, and any such liability could be extensive. We are also subject to substantial regulation relating to occupational health and safety, environmental protection, hazardous substance control, and waste management and disposal. The failure to comply with such regulations could subject us to, among other things, fines and criminal liability.

Certain chemotherapeutic agents that we employ in our aqueous-based protein systems, Anhydrous Delivery Vehicles, and regional delivery technology are known to have toxic side effects, particularly when used in traditional methods of administration. Each product incorporating a chemotherapeutic agent will require separate FDA approval as a new drug under the procedures specified above. Bovine collagen is a significant component of our protein matrix. Two rare autoimmune connective tissue conditions, polymyositis and dermatomyositis, have been alleged to occur with increased frequency in patients who have received cosmetic collagen treatments. Based upon the occurrence of these conditions, the FDA requested a major manufacturer of bovine collagen products for cosmetic applications to investigate the safety of such uses of its collagen. In October 1991, an expert panel convened by the FDA to examine this issue found no statistically significant relationships between injectable collagen and the occurrence of autoimmune disease, but noted that certain limitations in the available data made it difficult to establish a statistically significant association.

In addition, bovine sourced materials are of some concern because of transmission of Bovine Spongiform Encelphalopathy ("BSE"). We have taken all precautions to minimize the risk of contamination of our collagen with BSE, including the use of United States—sourced cow hides. The Committee For Proprietary Medicinal Products, a steering committee of the European Medicines Evaluation Agency, has classified materials made from bovine skin products as showing no detectable infectivity, indicating minimal risk of transmission of BSE.

## OUR STOCK PRICE IS VOLATILE; WE HAVE NOT DECLARED DIVIDENDS

The market prices for securities of biopharmaceutical and biotechnology companies (including us) have historically been highly volatile, and, in addition, the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Future announcements concerning us, our competitors or other biopharmaceutical products, governmental regulation, developments in patent or other proprietary rights, litigation or public concern as to the safety of products that we or others have developed and general market conditions may have a significant effect on the market price of our securities. We have not paid any cash dividends on our Common Stock and do not anticipate paying any dividends in the foreseeable future.

## RISKS ASSOCIATED WITH ANTI-TAKEOVER PROVISIONS

Certain provisions of our Certificate of Incorporation and Bylaws may make it more difficult for a third party to acquire, or discourage a third party from attempting to acquire, control of us. These provisions could limit the price that certain investors might be willing to pay in the future for shares of our Common Stock. Our Board of Directors has the authority to issue shares of Preferred Stock and to determine the price, rights, preferences, privileges and restrictions of those shares without any further vote or action by the stockholders.

The rights of the holders of Common Stock will be subject to, and may be adversely affected by, the rights of the holders of any Preferred Stock that may be issued in the future. The issuance of Preferred Stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire a majority of our outstanding voting stock. We have no present plans to issue shares of Preferred Stock. Certain provisions of Delaware law applicable to us could also delay or make more difficult a merger, tender offer or proxy contest involving us, including Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years unless certain conditions are met.

We are aware of the issues associated with the programming code in existing computer systems as the millennium year 2000 ("Y2K") approaches. The "year 2000" problem is pervasive and complex and many computer operations will be affected in some way by the rollover of the two digit year value to 00. Some computer systems may not properly recognize date sensitive information when the year changes to 2000. Systems that do not properly recognize such information could generate erroneous data or cause a system to fail.

We have formed a Year 2000 Task Force to determine what actions are required to resolve year 2000 issues. We are performing an internal systems assessment and we expect to complete any necessary conversion by the second quarter of 1999. We have determined that the related potential effect on our business, financial condition or results of operations are not expected to be material.

During 1997, we installed a new accounting system that the vendor confirmed addresses the year 2000 related issues. We have initiated formal communication with other significant vendors and suppliers to determine the extent to which the Company's operations are vulnerable to those third parties' failure to remediate their own Y2K issues. In the event that any of the Company's significant suppliers do not successfully achieve Y2K compliance, the Company's business or operations could be adversely affected. In addition, the Company may be vulnerable to external forces that might generally affect industry and commerce, such as utility and transportation company Y2K compliance failures and related service interruptions. There can be no assurance that the systems of other companies on which the Company's systems rely will be converted on a timely basis and would not have an adverse effect on the Company's operations.

We have not yet fully developed a comprehensive contingency plan to address situations that may result if any of the Company's significant vendors and suppliers are unable to achieve Y2K readiness of its critical operations. Development of such plan is in progress and is expected to be completed by the second quarter of 1999.

To date we have spent \$10,000 to rectify issues related to Y2K. At the current stage of the assessment process, we do not expect total projected costs of implementing year 2000 requirements to exceed \$100,000 which represents approximately 20% of the 1999 Information Technology budget.

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## MANAGEMENT

EXECUTIVE OFFICERS OF THE COMPANY

Certain information about the Company's executive officers is set forth below:

## <TABLE> <CAPTION>

NAME	AGE	POSITION
<s> Michael D. Casey</s>	<c> 53</c>	<c> Chairman, President and Chief Executive Officer</c>
David G. Ludvigson	48	Senior Vice President and Chief Financial Officer
Richard D. Leavitt, M.D.	53	Senior Vice President, Medical and Regulatory Affairs
Dennis M. Brown, Ph.D.	49	Vice President, Discovery Research
Richard E. Jones, Ph.D.	54	Vice President, Research and Development
Ronald P. Lucas	57	Vice President, Operations
Natalie L. McClure, Ph.D.	46	Vice President, Regulatory Affairs and Quality Assurance
Harry D. Pedersen	43	Vice President, Corporate Development

</TABLE>

Mr. Casey was appointed to the position of Chairman in February 1999 and has been President, Chief Executive Officer and a director of the Company since October 1997. From November 1995 to December 1996, he was Executive Vice President of Schein Pharmaceutical, Inc., ("Schein"), a generic and ethical pharmaceutical company, and in December 1996 he was appointed President of the retail and specialty products division of Schein. From June 1993 to November 1995, he served as President and Chief Operating Officer of Genetic Therapy,

Inc., a biopharmaceutical company. Mr. Casey was President of McNeil Pharmaceutical, a unit of Johnson & Johnson, from 1989 to June 1993 and Vice President, Sales and Marketing for the Ortho Pharmaceutical Corp. ("Ortho") subsidiary of Johnson & Johnson from 1985 to 1989. Previously, he held a number of sales and marketing positions with Ortho.

Mr. Ludvigson has been Senior Vice President and Chief Financial Officer since September 1998. From February 1996 to June 1998, he was President and Chief Operating Officer and a member of the Board of Directors of NeTpower Inc., a computer workstation company. From October 1993 to February 1996 he was Vice President and Chief Financial Officer of IDEC Pharmaceuticals Corporation, a biotechnology company. Previously, from 1992 to 1993, he was Vice President, Worldwide Sales and Marketing at Conner Peripherals, Inc., a manufacturer of computer storage equipment, and from 1988 to 1992, he held a series of senior management positions with MIPS Computer Systems, Inc. ("MIPS"), including, most recently, Executive Vice President, Chief Operating Officer and Chief Financial Officer. Prior to joining MIPS, he was an officer of System Industries, Inc., a computer storage systems supplier. He held a variety of financial management positions at Unisys/Burroughs Corp. and was a senior manager at Price Waterhouse.

Dr. Leavitt joined the Company in November 1996 as Senior Vice President, Medical and Regulatory Affairs. From June 1993 to November 1996, he was Vice President, Clinical and Regulatory Affairs of Focal Incorporated, a biopharmaceutical company. Prior to joining Focal Incorporated, from 1991 to June 1993 he served as Director, Clinical Research at Genetics Institute. Prior to joining Genetics Institute, from 1986 to 1991 he held various management positions at Fujisawa USA, Fujisawa SmithKline Corporation, and Centocor Incorporated. Prior to joining Centocor Incorporated, he was an Assistant Professor at the University of Maryland School of Medicine and Johns Hopkins University School of Medicine.

Dr. Brown, a founder of the Company, has been Vice President, Discovery Research since March 1995 and was Vice President of Scientific Affairs from 1985 to March 1995. He was also a director of Matrix from 1985 to 1991. From 1985 until 1987, he was an Assistant Professor of Radiology at the Joint Center for Radiation Therapy at Harvard Medical

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School. From 1979 to 1985, he was a Research Associate, Department of Radiology at the Stanford University School of Medicine.

Dr. Jones was named Vice President of Research and Development in October 1991. Prior to joining Matrix, he held the position of Vice President of Pharmaceutical Development at Pharmetrix Corporation, a biotechnology company, from 1989 to 1991. From 1988 to 1989, he held the position of Vice President of Development at Liposome Technology, Inc., a biotechnology company, and from 1984 to 1988 he was at Genentech, Inc. as Director, Pharmaceutical Research & Development and Acting Director, Pharmaceutical Manufacturing in 1985 and 1986. He held various positions at Syntex Research from 1969 to 1984.

Mr. Lucas became Vice President of Operations at Matrix in March 1996. From September 1994 to February 1996, he was the Vice President of Operations at Telios Pharmaceuticals ("Telios"), a division of Integra LifeSciences. Prior to joining Telios, he was the Vice President of Operations from January 1991 to September 1994 at IVAC Corporation, a division of Eli Lilly and Company. From 1986 to 1991, he was Director of Project Management and Director of Manufacturing Operations at Hybritech, Inc., a division of Eli Lilly. He also held a number of management and technical positions at Eli Lilly's corporate headquarters in Indianapolis.

Dr. McClure was named Vice President, Regulatory Affairs of the Company in March 1996. In September 1996, she also assumed responsibility for the Quality Assurance Group. Dr. McClure held the positions of Associate Director of Regulatory Affairs from January 1993 to August 1993 and Director of Regulatory Affairs from August 1993 to March 1996. Prior to joining Matrix, she held various positions at Syntex Corporation in the Chemical Process Development department and in Regulatory Affairs.

Mr. Pedersen was appointed Vice President, Corporate Development in June 1997. Between December 1995 and May 1997, he was Senior Director, Strategic Business Development, for Hoechst Marion Roussel. Between June 1992 and December 1995, he was Senior Director of Business Development for Marion Merrell Dow. Prior to that, he held a variety of positions with Marion Laboratories including Manager of European Licensing.

## ITEM 2. PROPERTIES

In March 1998, the Company entered into an agreement with a real estate investment trust for the sale and leaseback of its San Diego manufacturing facility structured as an \$18,425,000 purchase and a \$6,000,000 convertible loan

secured by specific manufacturing related building improvements. The lease has a term of 13 years with options to renew for up to 25 years. Net cash from the lease and loan agreement, after the payment of the existing mortgage and escrow and other related fees, totaled approximately \$13,798,000 and is being used to fund operating expenses and capital purchases.

In 1996, the Company entered into an agreement to lease out a portion of its San Diego manufacturing facility. The original lease had a term of two years ending July 1998 and the rental income during the two-year period totaled approximately \$2.9 million. The sublease was extended through April 1999 and will result in additional rental income of \$1,150,000.

During September 1997, the Company's management suspended further development and commercialization of AccuSite after being notified that the FDA did not approve AccuSite as a treatment for genital warts. Pursuant to the restructuring plan which was established in the third quarter of 1997, the Operations group relocated to the San Diego facility from its Northern California facilities during the fourth quarter of 1997. During the first quarter of 1998, the Company terminated its lease obligation on the manufacturing facility in San Jose and negotiated termination agreements for the manufacturing and storage facilities located in Milpitas, California. Costs associated with the termination of the leases and write-off of leasehold improvements for the leased facilities have been accrued in current liabilities on the balance sheet. See "Management Discussion and Analysis--Results of Operations."

In May 1994, the Company entered into an 18-year lease agreement beginning in January 1996, for a facility totaling approximately 50,000 square feet in Fremont, California. This facility includes administrative space and research and development space. This lease has an escalation clause in which the annual rent expense ranges from \$420,000 to \$1,034,000.

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#### ITEM 3. LEGAL PROCEEDINGS

None.

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

No matters were submitted to a vote of the Company's stockholders through solicitation of proxies or otherwise during the last quarter of the fiscal year ended December 31, 1998.

## PART II

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

The Common Stock of Matrix Pharmaceutical, Inc. trades on the Nasdaq National Market tier of the Nasdaq Stock Market under the symbol MATX. The Company's Common Stock began trading on January 28, 1992. The following table presents quarterly information on the high and low sale prices of the Company's Common Stock for fiscal years 1998 and 1997, as regularly quoted on the Nasdaq National Market.

<TABLE>

Fiscal Year	High	Low
<s> 1998</s>	<c></c>	<c></c>
1st Quarter 2nd Quarter 3rd Quarter 4th Quarter	\$ 5.44 5.75 4.38 4.00	\$ 3.25 3.88 1.75 2.13
1997		
1st Quarter 2nd Quarter 3rd Quarter 4th Quarter	\$ 7.50 7.84 7.44 5.00	\$ 5.75 5.00 3.94 3.00

</TABLE>

As of February 28, 1999, there were approximately 278 holders of record of the Company's Common Stock. No dividends have been paid on the Common Stock since the Company's inception, and the Company does not anticipate paying any dividends in the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA

<TABLE> <CAPTION>

</TABLE>

(In thousands except per share amounts)

								ember 31,			Inception (February 11, 1985) to December 31,
		1994		1995		1996		1997		1998	1998
<pre><s> CONSOLIDATED STATEMENT OF OPERATION DATA:</s></pre>	<c< th=""><th>&gt;</th><th></th><th></th><th></th><th></th><th><c></c></th><th></th><th></th><th></th><th><c></c></th></c<>	>					<c></c>				<c></c>
Revenues	\$	100	\$		\$		\$		\$		\$ 2,250
Costs and expenses											
Research and development In-license fee		17,072 		20,256		24,320		27 <b>,</b> 214		21,589	
General and administrative Special charges		3,806		8,336 		11,428		14,270 4,518		4,000 6,649 	53,884 4,518
Total costs and expenses		20,878		28,592		35,748		46,002		32,238	
Loss from operations Interest income Rental income Other income Interest expense										(32,238) 4,491 1,554 6,640	
Net loss	\$	(19,588)	\$	(26,617)	\$	(29,643)	\$	(39,731)	\$	(21,349)	\$ (166,969)
Basic and diluted net loss per common share  Weighted average shares used in computing basic and diluted net	\$	(1.86)			\$	(1.48)	\$	(1.85)	\$	(0.97)	
loss per common share											

10,538		12,173		20,081		21,336		22,033														
						cember 31,																
		1994		1995		1996		1997		1998												
``` SUMMARY OF CONSOLIDATED BALANCE SHEET DATA: ```								•														
Cash, cash equivalents and investments Total assets Total long-term liabilities Total stockholders' equity	\$	35,059 37,767 761 34,168	\$	77,331 94,419 12,307 76,355		114,584 134,950 11,724 115,511		80,368 110,429 22,161 76,653		66,545 83,731 19,131 55,872												
Period from

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

THIS FORM 10-K MAY CONTAIN, IN ADDITION TO HISTORICAL INFORMATION, FORWARD-LOOKING STATEMENTS, INCLUDING WITHOUT LIMITATION, STATEMENTS REGARDING THE TIMING AND OUTCOME OF REGULATORY REVIEWS AND CLINICAL TRIALS. ANY SUCH FORWARD-LOOKING STATEMENTS ARE BASED ON MANAGEMENT'S CURRENT EXPECTATIONS AND ARE SUBJECT TO A NUMBER OF RISKS AND UNCERTAINTIES THAT COULD CAUSE ACTUAL RESULTS TO DIFFER MATERIALLY FROM EXPECTED RESULTS. FOR ADDITIONAL INFORMATION, INCLUDING RISK FACTORS, SUCH AS NO ASSURANCE OF REGULATORY APPROVALS;

UNCERTAINTIES ASSOCIATED WITH CLINICAL TRIALS; HISTORY OF LOSSES; FUTURE PROFITABILITY UNCERTAIN; ADDITIONAL FINANCING REQUIREMENTS AND UNCERTAIN ACCESS TO CAPITAL MARKETS; LIMITED SALES AND MARKETING EXPERIENCE; LIMITED MANUFACTURING EXPERIENCE; DEPENDENCE ON SOURCES OF SUPPLY; RAPID TECHNOLOGICAL CHANGE; SUBSTANTIAL COMPETITION; UNCERTAINTY REGARDING PATENTS AND PROPRIETARY RIGHTS; UNCERTAINTY OF PHARMACEUTICAL PRICING; AND NO ASSURANCE OF ADEQUATE REIMBURSEMENT, PLEASE SEE THE "RISK FACTORS" SECTION INCLUDED IN THIS FORM 10-K AS WELL AS OTHER FACTORS DISCUSSED BELOW AND ELSEWHERE IN THIS REPORT.

The following discussion should be read in conjunction with the consolidated financial statements and related notes included on pages 31-45.

#### OVERVIEW

Since the Company's inception in 1985, the primary focus of its operations has been research and development and, to date, it has not received any revenues from the commercial sale of products. The Company has a history of operating losses and expects to incur substantial additional losses over the next several years as it continues to develop its current and future products. For the period from its inception to December 31, 1998, the Company has incurred a cumulative net loss of \$166,969,000.

RESULTS OF OPERATIONS

YEARS ENDED DECEMBER 31, 1998 AND 1997.

The Company had no revenues for 1998 or 1997.

Research and development expenses for 1998 decreased by 21% to \$21,589,000 as compared to \$27,214,000 for 1997. The decrease was primarily due to lower personnel costs, the suspension of clinical trials for AccuSite(TM) Injectable Gel and lower consulting expenses. The decrease was partially offset by higher depreciation expense and building rent expense in 1998 in connection with the sale and leaseback transaction for the San Diego manufacturing facility.

An in-license fee of \$4,000,000 was recorded during the third quarter of fiscal 1998 in connection with a new agreement to in-license a systemic anticancer agent known as FMdC which is in the early stages of clinical development. There were no license fees in the year ended 1997.

General and administrative expenses for 1998 decreased by 53% to \$6,649,000 compared to \$14,270,000 for 1997. The decrease was due primarily to lower litigation-related expenses, the absence of AccuSite-related product marketing expenses and lower personnel costs.

For 1998 no special charges were recorded as compared to special charges of \$4,518,000 which were recorded during the third quarter of fiscal 1997 in connection with the decision to suspend further development and commercialization of AccuSite. Management suspended the AccuSite program after the FDA notified the Company that it was not prepared to approve AccuSite as a treatment for genital warts. In September 1997, costs to conclude the clinical trials and commercial programs associated with AccuSite were accrued. The Company reduced its workforce by 63 employees, of which 46 positions related to manufacturing, resulting in severance expenses of \$1,478,000. Additional expenses included the write-off of inventory related to AccuSite of \$1,245,000, costs totaling \$1,194,000 associated with the shut down of the Company's Northern California facilities and write-off of manufacturing equipment, the closing of clinical trials with respect to AccuSite of \$414,000, and committed sales and marketing costs associated with AccuSite of \$187,000. At December 31, 1998, the remaining reserve balance of \$513,000 was included in current liabilities and is primarily for future cash payments related to facility lease costs.

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Interest income decreased by 20% to \$4,491,000 as compared to \$5,561,000 as a result of lower average cash balances during the year.

Other income increased to \$6,640,000 for 1998 as compared to \$352,000 for 1997 due primarily to the receipt of \$4,000,000 from a settlement with an insurance company, \$2,108,000 from the gain on sale and leaseback of the San Diego facility and \$560,000 from amortization of a five year non-compete agreement.

Interest expense increased by 62% to \$1,796,000 for 1998 as compared to \$1,109,000 for 1997 due to the impact of new building and equipment financing loans of \$10,000,0000 in the fourth quarter of 1997 and \$6,000,000 in 1998 offset by the payoff of the San Diego mortgage loan in the amount of \$9,840,000 in 1998.

As of December 31, 1998, the Company had federal and state net operating loss carryforwards of approximately \$165,400,000 and \$15,600,000,

respectively. The Company also had federal research and development tax credit carryforwards of approximately \$3,800,000. The federal net operating loss and credit carryforwards will expire at various dates beginning in the year 2000 through 2018, if not utilized. The state of California net operating loss and carryforwards will expire at various dates beginning in 1999 through 2004, if not utilized.

YEARS ENDED DECEMBER 31, 1997 AND 1996.

The Company had no revenues for 1997 or 1996.

Research and development expenses for 1997 increased by 12% to \$27,214,000 as compared to \$24,320,000 for 1996. This increase was primarily due to higher personnel costs for the Company's clinical and research and development programs as well as increases in personnel costs in anticipation of the commercial introduction of AccuSite in the United States. Higher clinical expenses related to IntraDose Injectable Gel in 1997 over 1996 were offset by lower clinical trial expenses for AccuSite in 1997.

General and administrative expenses for 1997 increased by 25% to \$14,270,000 as compared to \$11,428,000 for 1996. This increase was primarily due to higher legal expenses related to the Collagen litigation which was settled during the second quarter of 1997, increases in recruiting and relocation expenses, higher personnel costs, and product sales expenses associated with the commercial launch of Accusite in the United Kingdom during 1997.

Special charges of \$4,518,000, were recorded during the third quarter of fiscal 1997 in connection with the Company's decision to suspend further development and commercialization of AccuSite. These special charges included employee severance, write-off of inventory and manufacturing equipment, shut down of Northern California facilities, the closing of clinical trials with respect to AccuSite and sales and marketing associated with AccuSite. Management suspended the AccuSite program after being notified that the FDA was not prepared to approve AccuSite as a treatment for genital warts.

Rental income increased by 123% to \$1,467,000 for 1997 as compared to \$659,000 for 1996. The increase is primarily due to the full year effect of the sublease of a portion of the San Diego facility which commenced July 1996.

Interest income decreased by 15% to \$5,561,000 for 1997 from \$6,534,000 for 1996 as a result of lower average cash balances experienced throughout the year.

## LIQUIDITY AND CAPITAL RESOURCES

At December 31, 1998, the Company had \$66,545,000 in cash, cash equivalents and marketable securities, compared to \$80,368,000 at December 31, 1997. The decrease of \$13,823,000 reflects \$25,097,000 of cash disbursements used primarily to fund operating activities, including a \$4,000,000 in-license fee and \$4,000,000 of other income received from a settlement from an insurance company; payments of \$1,718,000 on debt and capital lease obligations; and capital purchases of \$1,016,000. This was partially offset by net cash receipts from the sale and leaseback of \$13,798,000.

In September 1998, the Company entered into an agreement to license a systemic anticancer agent known as FMdC for 4,000,000. The in-license fee was recorded in the third quarter of 1998 and was paid on October 22, 1998.

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In March 1998, the Company entered into an agreement with a real estate investment trust for the sale and leaseback of its San Diego manufacturing facility structured as an \$18,425,000 purchase and a \$6,000,000 convertible loan secured by specific manufacturing related building improvements. The lease has a term of 13 years with the option to renew up to 25 years. Net cash from the lease and loan agreement, after the payment of the existing mortgage and escrow and other related fees, totaled approximately \$13,798,000 and is being used to fund operating expenses and capital purchases.

In October 1997, the Company received \$10,000,000 before commitment fees, as part of a five-year equipment financing agreement maturing in 2002. The agreement is secured by equipment purchased by the Company between October 21, 1995 and March 31, 1998.

Special charges of approximately \$4,518,000 were recorded during the third quarter of 1997 in connection with the decision to suspend further development and commercialization of AccuSite. See "Results of Operations". Total cash payments in 1998 for restructuring were approximately \$1,550,000, and \$513,000 remained payable at December 31, 1998. The remaining amount is expected to be paid during the first half of 1999.

In September 1995, the Company repurchased from Medeva PLC all

marketing rights related to its AccuSite product for \$2,000,000, to be paid over a period of five years. As of December 31, 1998, the remaining balance of this obligation was \$1,000,000.

The Company has financed its operations and capital asset acquisitions from its inception through the sale of equity securities, interest income, and capital lease and debt financing. The Company expects to finance its continued operating requirements principally with cash on hand and marketable securities as well as additional capital that may be generated through equity and debt financings and collaborative agreements.

The Company's working capital and capital requirements will depend on numerous factors, including the progress of the Company's research and development programs, preclinical testing and clinical trial activities, the timing and cost of obtaining regulatory approvals, the levels of resources that the Company devotes to the development of manufacturing and marketing capabilities, technological advances and the status of competitors.

The Company expects to incur substantial additional costs relating to the continued clinical development of its oncology products, continued research and development programs, the development of manufacturing capabilities, and general working capital requirements. The Company anticipates that its existing and committed capital resources will enable it to maintain its current and planned operations at least through 2000. The Company may require additional outside financing to complete the process of bringing current products to market, and there can be no assurance that such financing will be available on favorable terms, if at all.

Capital expenditures for environmental control efforts were not material during the 1998 and 1997 fiscal years.

YEAR 2000

The Company is aware of the issues associated with the programming code in existing computer systems as the millennium year 2000 ("Y2K") approaches. The "year 2000" problem is pervasive and complex and many computer operations will be affected in some way by the rollover of the two digit year value to 00. Some computer systems may not properly recognize date sensitive information when the year changes to 2000. Systems that do not properly recognize such information could generate erroneous data or cause a system to fail.

The Company has formed a Year 2000 Task Force to determine what actions are required to resolve year 2000 issues. The Company is performing an internal systems assessment and expects to complete any necessary conversion by the second quarter of 1999. We have determined that the related potential effect on our business, financial condition or results of operations are not expected to be material.

During 1997, the Company installed a new accounting system that the vendor confirmed addresses the year 2000 related issues. We have initiated formal communication with other significant vendors and suppliers to determine the extent to which the Company's operations are vulnerable to those third parties' failure to remediate their own Y2K issues. In the event that any of the Company's significant suppliers do not successfully achieve Y2K compliance, the Company's

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business or operations could be adversely affected. In addition, the Company may be vulnerable to external forces that might generally affect industry and commerce, such as utility and transportation company Y2K compliance failures and related service interruptions. There can be no assurance that the systems of other companies on which the Company's systems rely will be converted on a timely basis and would not have an adverse effect on the Company's operations.

The Company has not yet fully developed a comprehensive contingency plan to address situations that may result if any of the Company's significant vendors and suppliers are unable to achieve Y2K readiness of its critical operations. Development of such plan is in progress and is expected to be completed by the second quarter of 1999.

To date the Company has spent \$10,000 to rectify issues related to Y2K. At the current stage of the assessment process, we do not expect total projected costs of implementing year 2000 requirements to exceed \$100,000 which represents approximately 20% of the 1999 Information Technology budget.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The Company's financial investment securities consist of certificates of deposit, commercial paper, master notes, and repurchase agreements. These securities all mature in 1999 and their estimated fair value approximates cost. The following table provides information about the Company's debt securities that are sensitive to changes in interest rates. The table presents principal

cash flows and related weighted-average interest rates by expected maturity dates.

<TABLE>

(dollars in thousands)	1999	2000	2001	2002	2003	Thereafte:	r Total	Fair Value 12/31/98
<pre><s> LIABILITIES Long-term Debt, including     Current Portion Fixed Rate</s></pre>	<c></c>	<c></c>	<c></c>	<c></c>	<c></c>	<c></c>	<c></c>	<c></c>
Imperial Bank Alexandria  Average Interest Rate	\$ 1,180 -  \$ 1,180 9.5%	\$ 1,291  \$ 1,291	\$ 1,416  \$ 1,416	\$ 4,868 6,000  \$ 10,868		- \$ -  - \$ -	\$ 6,000	\$ 6,000

</TABLE>

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

<TABLE>

Consolidated Balance Sheets--December 31, 1997 and 1998. Page 31

Consolidated Statements of Operations

Years Ended December 31, 1996, 1997 and 1998, and Period from

Inception (February 11, 1985) To December 31, 1998. Page 32

Consolidated Statement of Stockholders' Equity Period from Inception (February 11, 1985) To

December 31, 1998. Pages 33-34

Consolidated Statements of Cash Flows Years Ended December 31, 1992, 1993 and 1994, and Period

Years Ended December 31, 1996, 1997 and 1998, and Period from Inception (February 11, 1985) To December 31, 1998.

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Notes to Consolidated Financial Statements Pages 36-45

Report of Ernst & Young LLP, Independent Auditors Page 46

</TABLE>

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

None.

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PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information required by this item (with respect to Directors) is hereby incorporated by reference from the information under the caption "Election of Directors" contained in the Company's definitive Proxy Statement, to be filed with the Securities and Exchange Commission no later than 120 days from the end of the Company's last fiscal year in connection with the solicitation of proxies for its Annual Meeting of Stockholders to be held on May 4, 1999 (the "Proxy Statement"). The required information concerning Executive Officers of the Company is contained in Item 1, Part 1 of this Form 10-K under the caption "Executive Officers of the Company" on pages 18 and 19. The information required by Section 16(a) is incorporated by reference from the information under the caption "Compliance with Section 16(a) of the Securities Exchange Act of 1934" in the Proxy Statement.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference from the information under the caption "Election of Directors, Summary of Cash and Certain Other Compensation, Options and Stock Appreciation Rights, Option Exercises and Holdings" of 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 "Stock Ownership of Management and Certain Beneficial Owners" in the Proxy Statement.

#### ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required by this item is incorporated by reference from the information under the caption "Certain Relationships and Related Transactions" in the Proxy Statement.

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#### PART IV

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

## (a) FINANCIAL STATEMENTS

The following financial statements and supplemental data are filed as part of this Form 10-K. See Index to Consolidated Financial Statements under Item 8.

#### <TABLE>

<S> <C> Index to Consolidated Financial Statements: Consolidated Balance Sheets--December 31, 1997 and 1998. Page 31 Consolidated Statements of Operations Years Ended December 31, 1996, 1997 and 1998, and Period from Inception (February 11, 1985) To December 31, 1998. Page 32 Consolidated Statement of Stockholders' Equity Period from Inception (February 11, 1985) To December 31, 1998. Pages 33-34 Consolidated Statements of Cash Flows Years Ended December 31, 1992, 1993 and 1994, and Period Years Ended December 31, 1996, 1997 and 1998, and Period from Inception (February 11, 1985) To December 31, 1998. Page 35 Pages 36-45 Notes to Consolidated Financial Statements Report of Ernst & Young LLP, Independent Auditors Page 46

## </TABLE>

## (b) FINANCIAL STATEMENT SCHEDULES

All schedules are omitted because they are not applicable or are not required or the information required to be set forth therein is included in the consolidated financial statements or notes thereto.

## (c) REPORTS ON FORM 8-K

One Special Report on Form 8-K was filed during the quarter ended December 31, 1998. On October 28, 1998, the Company disclosed that it adopted an amendment to the Company's Stockholder Rights Plan ("the Plan") eliminating the "continuing director" provisions in such Plan.

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## (d) EXHIBITS

<TABLE> <CAPTION>

Number

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<S>

CC>

3.1 Certificate of Designation of Preferences of Preferred

Shares of the Company as filed with the Delaware Secretary of

State on August 25, 1994 (Incorporated by reference to Exhibit

5.3 filed with the Company's Form 8-K as filed with the

	Securities and Exchange Commission on September 27, 1994)
3.1(b)	Restated Certificate of Incorporation filed with the Delaware
	Secretary of State on August 13, 1992
3.2	Amended and restated bylaws.
3.3	Certificate of Designation of Preferences of Preferred Shares
	of the Company as filed with the Delaware Secretary of State
	on August 25, 1994 (Incorporated by reference to Exhibit 5.3
	filed with the Company's Form 8-K as filed with the Securities
	and Exchange Commission on September 27, 1994)
3.4	Certificate of Designations of Series B Junior Participating
	Preferred Stock of the Company filed with the Delaware
	Secretary of State on May 24, 1995 (Incorporated by reference
	to Exhibit 3.4 as filed with the Company's Form 10-Q for the
4 1	quarter ended June 30, 1995.)
4.1	Amended and Restated Registration Rights Agreement between the
	Company and the investors listed therein dated August 26, 1994
	(Incorporated by reference to Exhibit 5.2 filed with Company's
	Form 8-K as filed with the Securities and Exchange Commission
4 2	on September 27, 1994)
4.2	Rights Agreement between the Company and the First National
	Bank of Boston dated May 18, 1995 (Incorporated by reference
	to Exhibit No. 1 to the Company's Registration Statement on Form 8-A dated May 17, 1995).
10.1(a)	Series B Preferred Stock Purchase Agreement dated July 29,
10.1(a)	1987
10.2(a)	Series B Preferred Stock Purchase Agreement dated June 30,
10.2 (4)	1988
10.3(a)	Series C Preferred Stock Purchase Agreement dated May 24,
10.5(4)	1990
10.4(a)	Amendment Agreement dated May 24, 1990
10.5(a)	Stock Restriction Agreement between the Company and Edward E.
( /	Luck, dated July 29, 1987
10.6(a)	Stock Restriction Agreement between the Company and Dennis M.
, ,	Brown, Ph.D. dated July 29, 1987
10.7(a)	Agreement to Issue Warrant dated December 17, 1988
10.8(a)	Series B Preferred Stock Warrant issued to Western Technology
	Investment dated December 30, 1988
10.9(a)	Series B Preferred Stock Warrant issued to USX Credit
	Corporation dated December 30, 1988
10.10(a)	Series B Preferred Stock Warrant issued to Highline Financial
	Services, Inc. dated December 30, 1988
10.11(a)	Form of Common Stock Purchase Warrant
10.12(a)	Voting Agreement dated May 24, 1990, as amended
10.14(b)	Form of Restricted Stock Purchase Agreement
10.15(b)	Form of Stock Purchase Agreement (Repurchase Right with
	Escrow)
10.16(b)	Form of Stock Option Agreement
10.17(b)	Form of Stock Pledge Agreement
10.22(a)	Technology Assignment Agreement between the Company and Edward E. Luck and Dennis M. Brown, Ph.D. dated July 29, 1987
10 22/5/+	
10.23(a)*	Supply Agreement between the Company and **** dated December 22, 1988
10.25(c)	Form of Indemnification Agreement
10.26(d)	Form of Recapitalization
10.27 (b)	Lease between the Company and Becton Dickinson Corporation,
10.2/(2)	dated November 16, 1992
10.29(b)	Equipment Lease Agreement between the Company and General
**=* \**/	Electric Capital Corporation, dated December 17, 1992
10.30	Settlement Agreement and General Release dated February 2,
	1993 (Incorporated herein by reference to Exhibit 19.1 filed
	with the Company's Form 10-Q as filed with the Securities
	and Exchange Commission on May 14, 1993)
10.36*	Lease between the Company and Calaveras Associates II, dated
	August 4, 1993 (Incorporated herein by reference to the
	exhibit of the same number filed with the Company's Form 10-Q
	as filed with the Securities and Exchange Commission on
	November 12, 1993)

- (a) Incorporated herein by reference to the exhibits of the same number filed with the Company's Registration Statement on Form S-1 (File No. 33-44459) as filed with the Securities and Exchange Commission on December 19, 1991
- (b) Incorporated herein by reference to the exhibits of the same number filed with the Company's Form 10-K as filed with the Securities and Exchange Commission on March 31, 1993.
- (c) Incorporated herein by reference to the exhibit of the same number filed

 $<sup>^{\</sup>star}$   $\,\,$  Confidential treatment has been granted with respect to certain portions of this agreement.

with Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 33-44459) as filed with the Securities and Exchange Commission on January 23, 1992.

(d) Incorporated herein by reference to the exhibit of the same number filed with Amendment No. 2 to the Company's Registration Statement on Form S-1 (File No. 33-44459) as filed with the Securities and Exchange Commission on January 27, 1992.

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<table></table>	
<s></s>	<c></c>
10.38	Lease between the Company, John Arrillaga and Richard T. Peery Separate Property Trust, dated May 9, 1994 (Incorporated herein by reference to the exhibit of the same number filed
10.20	with the Company's Form $10-Q$ as filed with the Securities and Exchange Commission on August $12$ , $1994$ )
10.39	Investment Agreement by and between the Company and the investors listed therein dated August 26, 1994 (Incorporated herein by reference to Exhibit 5.1 filed with the Company's Form 8-K as filed with the Securities and Exchange Commission
10.40	on September 27, 1994) Equipment Lease Agreement between the Company and Financing For Science International, Inc. dated September 1, 1994 (Incorporated by reference to the exhibit of the same number
10.41	filed with the Securities and Exchange Commission on November 2, 1994) Form of Stock Purchase Agreement by and between the Company
10111	and the investors listed therein dated July 14, 1995 and July 21, 1995 (Incorporated by reference to Exhibit No. 4.1 to the registration Statement on Form S-3, Registration No. 33-94854, filed with the Securities and Exchange Commission on July 21, 1995, as amended)
10.42	Termination and Repurchase Agreement between the Company and Medeva dated September 18, 1995 (Incorporated by reference to exhibit No. 10.1 to the Company's Registration Statement on Form S-3 (file No. 33-96556) as filed with the Securities and Exchange Commission on September 25, 1995)
10.43	Equipment Lease Agreement between the Company and Lease Management Services, Inc. dated August 28, 1995 (Incorporated herein by reference to exhibit No. 10.3 filed with the Company's Form 10-Q as filed with the Security and Exchange
10.44	Commission on November 7, 1995) Contract of Purchase and Sale and Joint Escrow Instructions between the Company and the Federal Deposit Insurance Corporation dated November 2, 1995 (Incorporated herein by
10.45	reference to the exhibit of the same number filed with the Company's Form 10-K as filed with the Securities and Exchange Commission on March 1, 1996)  Industrial Multi-Tenant Lease agreement dated July 15, 1996 between the Company, as landlord and Advanced Tissue Sciences, Inc., as tenant filed herewith. (Incorporated herein by reference to the exhibit of the same number filed with the
	Company's Form $10-Q$ as filed with the Securities and Exchange Commission on August 8, 1996)
10.46*	Settlement and License Agreement effective as of May 23, 1997 by and between Collagen Corporation and the Company Distribution Agreement made as of August 4, 1997 by and
10.48(e)	between the Company and Altana, Inc. 1988 Restricted Stock Plan (Amended and Restated through March
10.49(f)	19, 1997) Form of Stock Issuance Agreement
10.50(g)	1991 Directors Stock Option Plan (Amended and Restated through March 19, 1997)
10.51(h)	Form of Non-Statutory Stock Option Agreement
10.52	Imperial Bank Credit Agreement date October 8, 1997 (Incorporated herein by reference to the exhibit of the same number filed with the Company's Form 10-K as filed with the Securities and Exchange Commission on March 27, 1998)
10.53	Option Acceleration Program dated January 27, 1998 (Incorporated herein by reference to the exhibit of the same number filed with the Company's Form 10-K as filed with the Securities and Exchange Commission on March 27, 1998)
10.54	Termination of Lease Agreement with Becton Dickinson (Incorporated herein by reference to the exhibit of the same number filed with the Company's Form 10-K as filed with the Securities and Exchange Commission on March 27, 1998)
10.55	Employment Agreement between the Company and Michael D. Casey (Incorporated herein by reference to the exhibit of the same number filed with the Company's Form 10-K as filed with the Securities and Exchange Commission on March 27, 1998)

10.56	Purchase and Sale Agreement and Joint Escrow Instructions by
	and between Alexandria Real Estate Equities, Inc. and Matrix
	Pharmaceutical, Inc. dated February 3, 1998 (Incorporated herein by
	reference to the exhibit of the same number filed with the Company's
	Form 10-0 as filed with the Securities and Exchange Commission on
	May 7, 1998)
10.57	Lease by and between ARE-4757 Nexus Centre, LLC and Matrix
	Pharmaceutical, Inc. dated March 25, 1998. (Incorporated herein by
	reference to the exhibit of the same number filed with the Company's
	Form 10-0 as filed with the Securities and Exchange Commission on
	May 7, 1998)
10.58	Loan and Security Agreement by and between ARE-4757 Nexus Centre,
10.30	LLC, and Matrix Pharmaceutical, Inc. dated March 25, 1998
	(Incorporated herein by reference to the exhibit of the same number
	filed with the Company's Form 10-0 as filed with the Securities and
	1 1
10.59	Exchange Commission on May 7, 1998)
10.59	Matrix Pharmaceutical, Inc. v. Chubb Customs Ins. Co., et al.
	Settlement Agreement (Incorporated herein by reference to the exhibit
	of the same number filed with the Company's Form 10-Q as filed with
10 604	the Securities and Exchange Commission on May 7, 1998)
10.60*	License Agreement by and between Hoechst Marion Roussel, Inc.
	and Matrix Pharmaceutical, Inc. dated September 22, 1998 (Incorporated
	herein by reference to the exhibit of the same number filed with the
	Company's Form 10-Q as filed with the Securities and Exchange
	Commission on November 10, 1998)
23.1	Consent of Ernst & Young LLP, Independent Auditors
27	Financial Data Schedule

- \* Confidential treatment has been granted with respect to certain portions of this agreement.
- (e) Incorporated by reference to Exhibit 99.1 of Registration Statement on Form S-8 (No. 333-32213).
- (f) Incorporated by reference to Exhibit 99.6 of Registration Statement on Form S-8 (No. 333-32213).
- (g) Incorporated by reference to Exhibit 99.7 of Registration Statement on Form S-8 (No. 333-32213).
- (h) Incorporated by reference to Exhibit 99.8 of Registration Statement on Form S-8 (No. 333-32213).

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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.

MATRIX PHARMACEUTICAL, INC.

Date: March 25, 1999

By: /s/ Michael D. Casey

-----

Michael D. Casey

President and Chief Executive Officer

## POWER OF ATTORNEY

## KNOW ALL PERSONS BY THESE PRESENTS:

That the undersigned officers and directors of Matrix Pharmaceutical, Inc., a Delaware corporation, do hereby constitute and appoint David G. Ludvigson the lawful attorney and agent, with power and authority to do any and all acts and things and to execute any and all instruments which said attorney and agent determines may be necessary or advisable or required to enable said corporation to comply with the Securities Exchange Act of 1934, as amended, and any rules or regulations or requirements of the Securities and Exchange Commission in connection with this Form 10-K. Without limiting the generality of the foregoing power and authority, the powers granted include the power and authority to sign the names of the undersigned officers and directors in the capacities indicated below to this Form 10-K, to any and all amendments, and to any and all instruments or documents filed as part of or in conjunction with this Form 10-K or amendments or supplements thereof, and each of the undersigned hereby ratifies and confirms all that said attorney and agent shall do or cause to be done by virtue hereof. This Power of Attorney may be signed in several counterparts.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated.

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.

<TABLE>

<s></s>		<c></c>

Date: March 25, 1999 /s/ Michael D. Casey

Michael D. Casev

Chairman, President and Chief Executive Officer (Principal Executive Officer)

Date: March 25, 1999 /s/ David G. Ludvigson

David G. Ludvigson

Senior Vice President and Chief Financial

Officer (Principal Financial and

Accounting Officer)

Date: March 25, 1999 /s/ J. Stephan Dolezalek

J. Stephan Dolezalek

Director

Date: March 25, 1999 /s/ Marvin E. Jaffe, M.D.

\_\_\_\_\_

Marvin E. Jaffe, M.D.

Director

Date: March 25, 1999 /s/ Bradley G. Lorimier

Bradley G. Lorimier

Director

/s/ Edward E. Luck Date: March 25, 1999

\_\_\_\_\_

\_\_\_\_\_

Edward E. Luck Director

Date: March 25, 1999 /s/ John E. Lyons

John E. Lyons Director

Date: March 25, 1999 /s/ Julius L. Pericola

\_\_\_\_\_

Julius L. Pericola

Director

Date: March 25, 1999 /s/ James R. Glynn

James R. Glynn Director

</TABLE>

MATRIX PHARMACEUTICAL, INC. (a development stage company)

CONSOLIDATED BALANCE SHEETS

<TABLE> <CAPTION>

(In thousands except share and per share amounts)

Other current assets

December 31,

1,378

2,657

		1997		1998 
<\$>	<c></c>		<c></c>	
ASSETS				
Current assets:				
Cash and cash equivalents	\$	19,719	\$	24,840
Short-term investments		40,666		41,705
Short-term notes from related parties		750		404

Total current assets	 62,513		69,606
Property and equipment, net	26,742		13,416
Non-current investments	19,983		
Long-term notes from related parties	600		600
Deposits and other assets	591		109
	\$ 110,429	\$ =====	83,731
LIABILITIES AND STOCKHOLDERS' EQUITY			
Current liabilities:			
Accounts payable	\$ 2,800	\$	1,276
Accruals for special charges	2,063		513
Accrued compensation	922		1,094
Accrued clinical trial costs	1,788		1,505
Other accrued liabilities	1,199		1,483
Current portion of deferred other income	560		560
Current portion of debt and capital lease obligations	2,283		2,297
Total current liabilities	 11,615		8,728
Debt and capital lease obligations, less current portion	20,248		14,176
Deferred other income	1,913		4,955
Total long-term liabilities	 22,161		19 <b>,</b> 131
Stockholders' equity:			
Common stock, \$0.01 par value per share; 30,000,000 shares authorized,			
21,908,300 shares issued and outstanding in 1997;			
22,154,710 shares issued and outstanding in 1998	219		220
Additional paid-in capital	224,925		•
Notes receivable from shareholders	(2,313)		(2,282)
Deferred compensation	(539)		(232)
Accumulated other comprehensive income (loss)	(19)		45
Deficit accumulated during the development stage	 (145,620)		(166 <b>,</b> 969)
Total stockholders' equity	76,653		55 <b>,</b> 872
	\$ 110,429	\$	83 <b>,</b> 731

(See accompanying notes )  $\,$ 

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MATRIX PHARMACEUTICAL, INC. (a development stage company)

CONSOLIDATED STATEMENTS OF OPERATIONS

<TABLE> <CAPTION>

(In thousands except per share amounts)

(February 11, 1985) to For the Years Ended December 31, December 31, 1997 1998 1998 <C> <C> <C> < \$ 2,250 Ś Revenues Costs and expenses 21,589 Research and development 24,320 27,214 In-license fee 4,000 4,000 14,270 6,649 53,884 General and administrative 11,428 Special charges 4,518 Total costs and expenses 35,748 46,002 32,238 200,560 \_\_\_\_\_ (35,748) (46,002) (32,238) (198,310) Loss from operations 5,561 1,467 4,491 1,554 6,640 25**,**320 6,534 Interest income 659 --3,680 6,992 Rental income Other income (1,796) (1,088)(1,109)(4,651) Interest expense Net loss \$ (29,643) \$ (39,731) \$ (21,349) \$ (166,969)

Period from Inception

Basic and diluted net loss per common share \$ (1.48) \$ (1.85) \$ (0.97)

Weighted average shares used in computing basic and diluted net

loss per common share 20,081 21,536 22,033

</TABLE>

(See accompanying notes )

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MATRIX PHARMACEUTICAL, INC. (a development stage company)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY For the period from inception (February 11, 1985) to December 31, 1998

<TABLE> <CAPTION>

(In thousands)

	Convertibl Preferred Stock			Notes Receiv- able from Share- holders		Other	-	Total Stock- holders' Equity
<\$>	<c> &lt;</c>	(C> <	<c></c>	<c></c>	<c> &lt;</c>	 <c></c>	<c></c>	<c></c>
Comprehensive loss:	()	()	()	\C>	(0)	()	<b>\(\)</b>	(0)
•	^	\$ -	s -	\$ -	^	^	â (40 COO)	A (40 600)
Net loss from inception (February 11, 1985) to December 31, 1994 Net unrealized gains (losses) on marketable	\$ -	Ş – _	۶ – _	Ş – _	\$ -	\$ - (670)	\$ (49,629)	\$ (49,629)
securities						(0,0)		(0,0)
Comprehensive loss								(50,299)
Complehensive 1055								(30,299)
Issuance of 508,867 shares of common stock	_	5	137	_	(55)	-	-	87
Issuance of 3,564,000 shares of common stock at								
\$15.00 per share, less offering costs, in an								
initial public offering in January 1992	_	36	48,950	_	_	_	_	48,986
Issuance of 5,250,000 shares of convertible	53	_	5,272	_	_	_		5,325
preferred stock			,					,
Recapitalization of the Company (259,524 shares								
of common stock converted to 3,500,000 shares of								
convertible preferred stock)	35	(3)	(32)	_	_	_	_	_
Issuance of 4,571,429 shares convertible								
preferred stock for cash and conversion of								
\$400,000 notes payable to stockholders (at \$1.75								
per share) in May 1990, net of offering costs	45	_	7,880	_	_	_	_	7,925
Conversion of 6,343,531 shares of convertible								
preferred stock to common stock at the time of								
the initial public offering (after 1-for-2.1								
reverse stock split in January 1992)	(133)	63	70	_	_	_	_	_
Issuance of 54,391 shares of common stock to								
employees and consultants for cash under stock								
option plan (from \$0.23 to \$0.37 per share)	_	1	13	_	_	_	_	14
Cancellation of promissory note in exchange for								
the repurchase of 238,095 shares of common stock								
from an officer in December 1990	_	(2)	(53)	_	55	_	_	_
Deferred compensation related to grant of stock	_		819	_	(819)	_	_	_
options								
Issuance of 59,757 shares of common stock to								
employees, consultants, and investors for cash								
under the stock option plan and for exercise of								
warrants (from \$0.23 to \$0.37 per share)	_	_	17	_	_	_	_	17
Issuance of 200,000 shares of common stock to								
Medeva PLC in May 1993 at \$15.00 per share, less								
offering costs	_	2	2,833	_	_	_	_	2,835
Issuance of 40,118 shares of common stock to								
employees and investors for cash under the stock								
option plan and for exercise of warrants (from								
\$0.23 to \$9.00 per share)	_	1	176	-	_	_	_	177
Issuance of 466,667 shares of common stock to								
Medeva PLC in May 1994 at \$15.00 per share, less								
offering costs	_	5	6,600	_	-	_	-	6,605
Issuance of 13,334 shares of convertible								
preferred stock in a private placement in August								

1994 at \$900 per share, less offering costs Amortization of deferred compensation	- -	- -	11,790 (12)	- -	- 718	- -	- -	11 <b>,</b> 790 706
Balance at December 31, 1994	\$ 	\$ 108	\$ 84,460	\$ 	\$ (101)	\$ (670)	\$ (49,629)	\$ 34,168
Comprehensive loss:								
Net loss	-	-	_	-	-	_	(26 <b>,</b> 617)	(26 <b>,</b> 617)
Net unrealized gains (losses) on marketable	-	-	-	-	-	358	-	358
Comprehensive loss								(26,259)
Issuance of 148,016 shares of common stock to employees and investors for cash under the stock option plan and for exercise of warrants (from								
\$0.23 to \$11.38 per share) Issuance of 10,800 shares to employees at \$14.00	-	1	425	-	-	-	-	426
per share	_	_	151	_	_	_	_	151
Issuance of 1,481,982 shares of common stock for cash in a private placement in August 1995 at \$12			101					101
per share, less offering costs Issuance of 4,097,000 shares of common stock for cash in a follow-on public offering in October	-	15	16,804	-	-	-	=	16,819
1995 at \$13.25 per share, less offering costs	-	41	50,908	-	-	-	-	50,949
Deferred compensation related to grant of stock options	_	_	514	_	(514)	_	_	_
Amortization of deferred compensation	-	-	-	-	101	-	-	101
Balance at December 31, 1995	\$ 	\$ 165	\$153,262	\$ 	\$ (514)	\$ (312)	\$ (76,246)	\$ 76 <b>,</b> 355

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MATRIX PHARMACEUTICAL, INC. (a development stage company)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY For the period from inception (February 11, 1985) to December 31, 1998

<TABLE> <CAPTION>

(In thousands)

	Conver Prefe Stoc	rred	Со		Additional	Sha	vable m re-	Deferred Compen-	lated Other Compre-		
<s></s>	<c></c>		<c></c>			<c></c>		<c></c>		<c></c>	<c></c>
Balance at December 31, 1995	\$	-	\$	165	\$ 153,262	\$	-	\$ (514)	\$ (312)	\$ (76,246)	\$ 76 <b>,</b> 355
Comprehensive loss: Net loss Net unrealized gains (losses) on marketable		-		-	-		-	-	-	(29,643)	
securities		-		-	-		-	_	236	_	236
Comprehensive loss											(29,407)
Issuance of 269,446 shares of common stock to employees and investors for cash under the stock option plan (from \$0.23 to \$13.50 per share)  Issuance of 3,162,500 shares of common stock for cash in a follow-on public offering in April		-		3	1,395		-	-	-	-	1,398
1996 at \$22.63 per share, less offering costs Conversion of 13,334 shares of convertible preferred stock into 1,333,400 shares of		-		32	67,336		_	-	-	-	67,368
common stock Deferred compensation related to grant of certain		-		13	(357	)	-	-	-	-	(344)
stock options Amortization of deferred compensation		-		_	407		-	(407) 141	_	_	- 141
Balance at December 31, 1996	\$	-	\$	213	\$ 222,043	\$	-	\$ (780)	\$ (76)	\$ (105,889)	\$ 115,511
Comprehensive loss: Net loss Net unrealized gains (losses) on marketable		-		-	-		-	-	-	(39,731)	(39,731)
securities		-		-	-		-	-	57	_	57
Comprehensive loss											(39,674)

Issuance of 208,862 shares of common stock to									
employees and investors for cash under the									
stock option plan (from \$0.23 to \$.37 per			0	7.4					7.6
share) Issuance of 71,582 shares to employees under		-	2	74	_	_	_	_	76
employee savings and retirement plan (from									
\$4.94 to \$6.69 per share)		_	_	427	_	_	_	_	427
Issuance of 370,000 shares to officers and				72/					727
employees for promissory notes under Shared									
Investment Program (\$6.25 per share)		_	4	2,309	(2,313)	_	_	_	_
Forfeitures of deferred compensation		_	_	(576)		576	_	_	_
Deferred compensation related to grant of certain									
stock options		-	_	648	_	(648)	_	_	_
Amortization of deferred compensation		-	-	-	-	313	-	_	313
Balance at December 31, 1997	\$		\$ 219	\$ 224,925	\$(2,313)	\$ (539)	\$ (19)	\$(145,620)	\$ 76 <b>,</b> 653
Comprehensive loss:									
Net loss		-	-	_	-	-	-	(21,349)	(21,349)
Net unrealized gains (losses) on marketable									
securities		-	-	-	-	-	64	_	64
Comprehensive loss									(21,285)
T									
Issuance of 165,384 shares of common stock to employees and investors for cash under the									
stock option plan (from \$0.231 to \$3.94 per									
share)		_	1	71	_	_	_	_	72
Issuance of 81,026 shares to employees under			_	7 1					, 2
employee savings and retirement plan (from \$2.62)	5								
to \$4.625 per share)		_	_	309	_	_	_	_	309
Amortization of deferred compensation		_	_	_	_	184	_	_	184
Forfeitures of deferred compensation		-	_	(123)	-	123	_	-	_
Repayment of notes receivable from shareholders		-	_	_	31	_	_	_	31
Treasury stock		_	_	(92)	_	_	_	-	(92)
Balance at December 31, 1998	\$		\$	\$ 225,090				\$ (166,969)	

(See accompanying notes)

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MATRIX PHARMACEUTICAL, INC. (a development stage company)

CONSOLIDATED STATEMENTS OF CASH FLOWS
Increase (Decrease) in Cash and Cash Equivalents

<TABLE>

		For the Years Ended December 31,						Period from Inception Pebruary 11, 1985) to ecember 31,
		1996		1997		1998		1998
<s></s>	<c></c>		<c></c>		<c></c>			
Cash flows used in operating activities:								
Net loss	\$	(29,643)	\$	(39,731)	\$	(21,349)	\$	(166,969)
Adjustments to reconcile net loss to net cash used by								
operating activities:								
Depreciation and amortization		1,051		1,142		2,259		7,868
Amortization of deferred compensation		141		313		184		1,457
Amortization of deferred income						(560)		(560)
Gain on sale & leaseback transaction						(1,882)		(1,882)
Repurchase of marketing rights		(250)		(250)		(500)		1,000
Other		83		72		218		718
Changes in assets and liabilities:								
Other current assets		(2,089)		1,663		(1,279)		(2,657)
Deposits and other assets		44		(418)		482		(118)
Notes receivable from related parties				(1,350)		346		(1,004)
Accounts payable		1,031		164		(1,524)		1,276
Accrued compensation		201		(123)		172		1,094
Deferred other income				2,473		(177)		2,296
Restructuring costs				2,063		(1,550)		513

Accrued clinical trial costs Other accrued liabilities		(575) 1,471	549 (936)	(283) 346		1,505 1,545
Net cash used in operating activities  Cash flows from investing activities:	(	28 <b>,</b> 535)	 (34,369)	 (25 <b>,</b> 097)		(153,918)
Capital expenditures		(2,326)	(9,857)	(1,016)		(32,670)
Proceeds from sale of fixed assets				17,744		17,744
Investment in securities	(1	89,548)	(31, 100)	(23,763)		(429,573)
Proceeds from sale of available-for-sale securities		95 <b>,</b> 219				221,101
Maturities of securities		21,734	65,000	42,707		166,415
Net cash flows provided by (used in) investing			 	 		
activities	(	74,921)	24,043	35,672		(56,983)
Cash flows from financing activities:						
Repayment of mortgage loan from sale				(9,840)		(9,840)
Payments on debt and capital lease obligations		(503)	(546)	(1,718)		(4,390)
Issuance of convertible promissory notes payable to						
stockholders						400
Net cash proceeds from issuance of:						
Debt and capital lease financing			9,950	6,000		28,835
Repayment of notes receivable from shareholders				32		32
Preferred stock						24,679
Common stock		68,422	503	72		196,025
Net cash flows provided by (used in) financing						
activities		67 <b>,</b> 919	9,907	(5,454)		235,741
Net increase (decrease) in cash and cash equivalents	(	35,537)	(419)	5,121		24,840
Cash and cash equivalents at the beginning of period		55 <b>,</b> 675	20,138	19,719		
Cash and cash equivalents at the end of period	\$	20 <b>,</b> 138	 19,719	24,840	\$	24,840
Supplemental schedule of noncash investing and	=======	=======	 	 ========		
financing activities:						
Notes receivable from shareholders in exchange for						
capital stock	\$		\$ 2,313	\$ 	\$	2,313
Financing of capital equipment			943			943
Issuance of stock upon conversion of						
promissory notes payable to stockholders						425
Supplemental disclosure of cash flow information:	\$ \$	1,088	\$ 1,229	\$ 1,669	===== \$	4,644

(See accompanying notes)

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MATRIX PHARMACEUTICAL, INC. (A DEVELOPMENT STAGE COMPANY)

NOTES TO CONSOLIDATED FINANCIAL STATMENTS

## 1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

BASIS OF PRESENTATION. Matrix Pharmaceutical, Inc. (the "Company") was incorporated in California on February 11, 1985 and reincorporated in Delaware in January 1992. The Company's principal activities to date have involved research and development of drug delivery systems using proprietary technology, in-licensing of a product candidate, recruiting key personnel, establishing a manufacturing process and raising capital to finance its development operations. The Company is classified as a development stage company.

In the course of its development activities, the Company has sustained continuing operating losses and expects such losses to continue over the next several years. The Company has financed its operations and capital acquisitions primarily through stock issuances, capital leases, and subsequent to 1996, by long-term debt.

PRINCIPLES OF CONSOLIDATION. The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary after elimination of all material intercompany balances and transactions.

CASH AND CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS. The Company invests its excess cash in government and corporate debt securities. Highly liquid investments with maturities of three months or less at the date of acquisition are considered by the Company to be cash equivalents. All other investments are reported as short-term investments.

MARKETABLE SECURITIES AVAILABLE- FOR- SALE. All marketable securities are classified as available-for-sale. Available-for-sale securities are carried at fair value, with unrealized gains and losses reported as a separate component of stockholders' equity. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretions of discounts to

maturity. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other than temporary for available-for-sale securities are included in interest and other expense. The cost of securities sold is based on the specific identification method.

DEPRECIATION AND AMORTIZATION. The Company depreciates property and equipment using the straight-line method over the assets' estimated useful lives. Building and improvements are depreciated over 25 years. Laboratory, operating and office equipment and furniture are depreciated over 10 years and computer equipment over five years. Leasehold improvements are depreciated over the shorter of the estimated useful life or the lease term. Amortization of equipment under capital leases is included with depreciation expense.

STOCK BASED COMPENSATION. Statement of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123"), encourages, but does not require, companies to record compensation costs for stock-based employee compensation plans at fair value. The Company has elected to continue to account for stock-based compensation using the intrinsic value method prescribed in Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" ("APB 25"), and related Interpretations. Accordingly, compensation costs for stock options granted to employees and directors is measured as the excess, if any, of the quoted market price of the Company's stock at the date of the grant over the amount an employee must pay to acquire the stock. Note 13 to the Consolidated Financial Statements contains a summary of the pro forma effects to reported net loss and per share data for 1996, 1997 and 1998 as if the Company had elected to recognize compensation cost based upon the fair value of options granted at grant date as prescribed by SFAS 123.

NET LOSS PER SHARE. Basic and diluted earnings per share have been calculated using the weighted average common shares outstanding during the periods in accordance with Statement of Financial Accounting Standards No. 128, "Earnings Per Share" ("SFAS 128") issued by the Financial Accounting Standards Board and Securities and Exchange Commission Staff Accounting Bulletin ("SAB No. 98").

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Net loss per common share is computed using the weighted average number of common shares outstanding. Common equivalent shares from stock options and warrants are not included in the per share calculations because their inclusion would be antidilutive.

NEW ACCOUNTING PRONOUNCEMENTS. The Company adopted Statement of Financial Accounting Standards No. 131, "Disclosure about Segments of an Enterprise and Related Information" ("SFAS 131"), at December 31, 1998. SFAS 131 establishes annual and interim reporting standards for an enterprise's operating segments and related disclosures about its products, services, geographic areas and major customers. Under SFAS 131, the Company's operations are treated as one operating segment as it only reports profit and loss information on an aggregate basis to chief operating decision makers of the Company.

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 amounts reported in the financial statements and accompanying notes. Actual results could differ from these estimates.

## 2. FINANCIAL INSTRUMENTS

The following is a summary of available-for-sale securities:

<TABLE> <CAPTION>

(IN THOUSANDS) Available-For-Sale Securities

December 31, 1998	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<s></s>	<c></c>	<c></c>	<c></c>	<c></c>
Certificates of deposit	\$ 41,615	\$ 98	\$ (8)	\$ 41,705
Commercial paper	13,100			13,100
Master notes	8,000			8,000
Repurchase agreements	2,475			2,475
	\$ 65,190	\$ 98	\$ (8)	\$ 65,280

<CAPTION>

(IN THOUSANDS) Available-For-Sale Securities

December 31, 1997	Cost	Uni	Gross Unrealized Gains		Gross Unrealized Losses		timated Fair Value
<s></s>	<c></c>	<c></c>		<c></c>		<c></c>	
U.S. government securities	\$ 38,49	0 \$	76	\$	(18)	\$	38,548
Certificates of deposit	25,09	9	1		(17)		25,083
Commercial paper	13,30	0					13,300
Master notes	1,68	7					1,687
Repurchase agreements	33	8					338
	\$ 78,91	4 \$	77	\$	(35)	\$	78 <b>,</b> 956

Included in cash equivalents at December 31, 1998 and 1997 are \$23,575,000 and \$18,307,000, respectively, of available-for-sale securities. The Company invests in repurchase agreement securities which are collateralized by U.S. government securities which have a market value of 102% of the investment. The securities are marked to market daily to ensure that the market value of the underlying assets remain sufficient. All available-for-sale securities have maturities of less than one year and cost approximates fair value.

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#### 3. GAIN ON SALE AND LEASEBACK TRANSACTION

In March 1998, the Company completed an agreement with a real estate investment trust for the sale and leaseback of its San Diego office/laboratory and manufacturing facility and an adjacent parcel of land. The transaction was structured as an \$18,425,000 sale and a \$6,000,000 convertible loan secured by specific manufacturing related building improvements. Under the terms of the agreement, the Company will lease the facility for 13 years with options to renew up to an additional 25 years. Matrix will pay an average \$2,800,000 in annual lease expense. Currently, this rental expense is partially offset by rental income from a portion of the facility leased to another bio-pharmaceutical company whose original lease expired July 31, 1998. The sublease was extended through April 1999 which is expected to result in additional rental income of \$1,150,000. The Company is currently seeking to rent this portion of the facility following the expiration of the existing lease. Net cash from the lease and loan agreement, after the payment of the existing mortgage and escrow and other related fees, totaled approximately \$13,798,000 and will be used to fund operating expenses and capital purchases. The total gain on the transaction is 5,769,000 of which 1,882,000 has been recognized during the year ended December 31, 1998 as an immediate gain while the remaining balance has been deferred and is being recorded to income over the 13-year lease term.

## 4. OTHER INCOME

Other income during 1998 of 6,640,000 includes the receipt of 44,000,000 from a settlement with an insurance company, 2,108,000 from the gain on sale and leaseback of the San Diego facility and 560,000 from amortization of a five year non-compete agreement.

## 5. REPURCHASE OF MARKETING RIGHTS

In September 1995, the Company repurchased from Medeva PLC all marketing rights related to its AccuSite product for \$2,000,000, to be paid over a period of five years. As of December 31, 1998 the obligation has a balance of \$1,000,000 and is included in current and long-term obligations on the balance sheet.

## 6. PROPERTY AND EQUIPMENT

Property and equipment is stated at cost and consists of the following:

(IN THOUSANDS)

<TABLE>

December 31,	1997	1998
	<c></c>	<c></c>
Land	\$ 4,258	\$
Building	6,928	
Leasehold improvements	8,734	8,970
Laboratory and operating equipment	7,219	6,177
Office and computer equipment	3,413	3,381
Manufacturing start-up costs	490	

In December 1995, the Company purchased a research and manufacturing facility in San Diego, California for \$13,100,000.

3.8

In March 1998, the Company completed an agreement with a real estate investment trust for the sale and leaseback of its San Diego office/laboratory and manufacturing facility and an adjacent parcel of land. The transaction was structured as an \$18,425,000 purchase and a \$6,000,000 convertible loan secured by specific manufacturing related building improvements.

The Company refinanced several of its existing operating leases in the fourth quarter 1997. As the new leases were recorded as capital leases, additional laboratory and operating equipment and office and computer equipment of \$900,000, together with a corresponding capital lease obligation, were recorded as of December 31, 1997.

#### 7. DEBT AND CAPITAL LEASE OBLIGATIONS

As noted in Footnote 3, the Company completed an agreement with a real estate investment trust for the sale and leaseback of its San Diego office/laboratory and manufacturing facility and an adjacent parcel of land. The transaction was structured as an \$18,425,000 sale and a \$6,000,000 convertible loan secured by specific manufacturing related building improvements. The loan bears interest at 11% per annum and the entire principal balance is due on March 26, 2002. The Company has the right prior to the maturity date to cause Lender to convert the loan to a lease agreement based upon the attainment of certain strategic alliances or joint ventures with a cumulative value in excess of \$15,000,000 as measured by initial and milestone payments. In the event the Company meets certain milestones and chooses to exercise this option, rent shall be increased by \$660,000 per year from approximately \$1,920,000 as per the lease agreement.

Assets purchased under debt (installment notes) or capital lease financing arrangements consist of building and related improvements, leasehold improvements, laboratory, operating, office and computer equipment with a cost of approximately \$16,749,000 and \$3,677,000 at December 31, 1997 and 1998, respectively. Accumulated depreciation of these assets totaled approximately \$2,772,000 and \$2,603,000 at December 31, 1997 and 1998, respectively. The weighted average interest rate for debt and capital lease obligations in 1998 was 9.52%.

In October 1997, the Company entered into a five-year equipment financing agreement for \$10,000,000. The loan bears 9% interest per annum and matures in 2002. The agreement is secured by equipment purchased by the Company between October 21, 1995 and March 31, 1998 with a cost of \$6,183,000.

Future payments under capital leases, are as follows at December 31,  $\,$ 

1998:

<TABLE>

(IN THOUSANDS)

Years ending December 31,	Capital Lease Obligations
<pre></pre>	<c> \$ 657 40 40 35 8</c>
Less amount representing interest	780 62
Present value of net minimum payments Current portion	718 616
Amounts due after one year	\$ 102

Future payments under debt obligations, are as follows at December 31,  $\,$ 

1998:

<TABLE> <CAPTION>

(IN THOUSANDS)

Installment Years ending December 31, \_\_\_\_\_\_ <S> <C> 1,180 1999 Ŝ 2000 1,291 2001 1,416 2002 10,868 2003 14.755 1,180 \_\_\_\_\_\_ Amounts due after one year \$ 13.575 \_\_\_\_\_\_

#### </TABLE>

## 8. OPERATING LEASE COMMITMENTS

The Company leased facilities in Fremont, San Jose, Milpitas and San Diego in the State of California. Rent expense under all of these arrangements was approximately \$1,610,000 in 1996, \$1,764,000 in 1997 and \$2,346,000 in 1998. Non-cancellable rental commitments under building and equipment operating leases are as follows at December 31, 1998:

<TABLE> <CAPTION>

### (IN THOUSANDS)

Years ending December 31,	Total
<s>&lt;</s>	<c></c>
1999	\$ 2,663
2000	2,559
2001	2,589
2002	2,619
2003	2,650
Thereafter	26,592
Total minimum lease payments	\$ 39 <b>,</b> 672

## </TABLE>

During September 1997, the Company's management suspended further development and commercialization of AccuSite after being notified that the FDA did not approve AccuSite as a treatment for genital warts. Pursuant to the restructuring plan which was established in the third quarter of 1997, the Operations group relocated to the San Diego facility from its Northern California facilities during the fourth quarter of 1997.

The Company entered into an eighteen-year lease agreement beginning in January 1996, for a facility totaling approximately 50,000 square feet in Fremont, California. This facility includes administrative, and research and development usage. This lease has an escalation clause in which the annual rent expense ranges from \$420,000 to \$1,034,000.

The Company entered into an agreement with a real estate investment trust for the sale and leaseback of its San Diego manufacturing facility in March 1998. The lease has a term of 13 years with options to renew for up to 25 years in which the annual rent expense ranges from \$1,920,000 to \$2,373,000.

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## 9. SPECIAL CHARGES

Special charges of \$4,518,000 were recorded during the third quarter

of 1997 in connection with the decision to suspend further development and commercialization of AccuSite. No special charges were recorded in 1998. Management suspended the AccuSite program after the FDA notified the Company that it was not prepared to approve AccuSite as a treatment for genital warts. In September 1997, restructuring costs to conclude the clinical trials and commercial programs associated with AccuSite were accrued. The Company reduced its workforce by 63 employees, of which 46 positions related to manufacturing, resulting in severance expenses of \$1,478,000. Additional expenses included the write-off of inventory related to AccuSite of \$1,245,000, costs totaling \$1,194,000 associated with the shut down of the Company's Northern California facilities and write-off of manufacturing equipment, the closing of clinical trials with respect to AccuSite of \$414,000, and sales and marketing costs associated with AccuSite of \$187,000. At December 31, 1998, the reserve balance of \$513,000 was included in current liabilities and is primarily for future cash payments related to facility lease costs.

#### 10. LITIGATION

On December 21, 1994, Collagen Corporation ("Collagen") filed a lawsuit against the Company in Santa Clara County Superior Court alleging misappropriation of trade secrets concerning the Company's manufacturing process for collagen and seeking unspecified damages and injunctive relief. The Company denied all allegations of the complaint and subsequently filed a cross-complaint against Collagen and Howard Palefsky, Collagen's former Chairman and Chief Executive Officer, seeking recovery of damages for defamation and violations of state law unfair competition.

On May 23, 1997, the lawsuit between the parties was settled on mutually agreeable terms and dismissed with prejudice. All claims by and against all parties have been released. Matrix agreed that for a period of five years it shall not manufacture or sell products directly competitive with Collagen's current core products. Collagen has granted Matrix a non-exclusive license to certain Collagen intellectual property for certain non-monetary consideration.

#### 11. DEFERRED OTHER INCOME

In June 1997, the Company received \$2,800,000 as part of a five-year non-compete agreement. This amount is amortized to other income over the duration of the agreement. At December 31, 1998, the remaining balance of \$1,913,000 was included in deferred other income in current liabilities and long-term obligations.

## 12. STOCKHOLDERS' EQUITY

PREFERRED SHARE PURCHASE RIGHTS PLAN. On April 17, 1995, the Company's Board of Directors adopted a Preferred Share Purchase Rights Plan under which stockholders receive one one-hundredth Series B junior participating preferred share purchase rights for each share of Matrix common stock. The rights will be distributed as a non-taxable dividend, will expire on May 28, 2005, and will be exercisable only if a person or group acquires 20% or more of the Company's common stock or announces a tender offer for 20% or more of the Company's common stock. The Board of Directors designated 150,000 shares as Series B junior participating preferred stock. As of December 31, 1998, no shares were issued or outstanding.

## 13. STOCK OPTION PLANS

1991 DIRECTORS STOCK OPTION PLAN. The Board of Directors adopted a Directors Stock Option Plan (the "Directors Plan") in 1991. Under the Directors Plan, each individual who first becomes a non-employee member of the Board of Directors is automatically granted a non-statutory option to purchase 40,000 shares of common stock which vest over a three-year period. Each non-employee director (upon re-election to the Board) will automatically receive an option to purchase 3,000 shares of common stock which vest over a one-year period. In May 1994, an additional 200,000 shares were reserved for issuance pursuant to the Directors Plan. In March 1997 the Director's Plan was amended such that all vested, unexercised options would remain outstanding for the full 10-year option term, regardless of whether the optionee continued to serve on the board. At the same time, an additional 250,000 shares were reserved for issuance under the Director's Plan. The aggregate maximum number of shares which may be issued under the automatic option grant

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program is 592,858 shares. At December 31, 1998, the total number of common shares reserved for issuance under director's stock options was 592,858, of which 250,635 were exercisable and 231,033 remain available for grant. In 1998 12,000 shares were granted.

1988 RESTRICTED STOCK PLAN. The Company's 1988 Restricted Stock Plan ("the Plan") permits the Company to (i) grant incentive options at 100 percent of fair

value at the date of grant; (ii) grant non-qualified options at 85 percent of fair value or greater; and (iii) grant purchase rights authorizing the sale of common stock at 85 percent of fair value subject to stock purchase agreements. Options may become exercisable immediately or in installments over time as specified in each option agreement. Shares purchasable under immediately exercisable options and under purchase rights may be subject to repurchase by the Company in the event of termination of employment; the Company's repurchase right shall lapse in one or more installments over the purchaser's period of service. The term of the Plan is ten years. Options have a maximum term of ten years, except options granted to ten-percent stockholders which have a maximum term of five years. In May 1994, an additional 450,000 shares of common stock were reserved for issuance pursuant to the Plan. In May 1996, an additional 850,000 shares of common stock were reserved for issuance pursuant to the Plan. In June 1997, an additional 2,000,000 shares were reserved for issuance pursuant to the Plan. At December 31, 1998, the total number of common shares reserved for issuance under restricted stock options was 4,630,953 of which 819,836 remain available for grant.

SHARED INVESTMENT PROGRAM. In March 1997, the Board of Directors authorized a special risk sharing arrangement designated as the Shared Investment Program ("the Program"). Under the Program, the Company's executive officers and other key managerial personnel were given the opportunity to purchase shares of Common Stock in an individually designated amount per participant determined by a Committee of the Board of Directors. A total of 370,000 shares were purchased under the Program by nine eligible employees at \$6.25 per share, the fair market value of the Common Stock on June 25, 1997, for an aggregate consideration of \$2,312,500. The purchase price was paid through the participant's delivery of a full-recourse promissory note payable to the Company. Each note bears interest at 6.69% compounded semi-annually and has a maximum term of nine years. The notes are secured by a pledge of the purchased shares with the Company. The Company recorded notes receivables from participants in this program for \$2,312,500 in the equity section in the Consolidated Balance Sheet.

Activity under the 1988 Restricted Stock Plan is as follows:

<TABLE>

		ailable outstanding		Price per	Weighted average exercise price			
<\$>	<c></c>	<c></c>	<c></c>				<c></c>	
Balances at December 31, 1995	26,490	1,466,990	\$	0.23 -	\$	15.00	\$	7.18
Additional authorization	850,000	·						
Grants of options	(1,214,050)	1,214,050	\$	6.16 -	\$	26.00	\$	10.42
Exercise of options		(223,588)	\$	0.23 -	\$	13.50	\$	4.04
Forfeitures	585,816	(585,816)	\$	5.63 -	\$	26.00	\$	14.15
Balances at December 31, 1996	248,256	1,871,636	\$	0.23 -	\$	21.00	\$	7.47
Additional authorization	2,000,000							
Shared investment program shares	(370,000)		\$	6.25 -	\$	6.25	\$	6.25
Restricted stock awards	(185,000)	185,000	\$	0.00 -	\$	0.00	\$	0.00
Grants of options	(3,030,584)	3,030,584	\$	3.50 -	\$	6.69	\$	4.37
Exercise of options		(208,862)	\$	0.23 -	\$	0.37	\$	0.36
Forfeitures	2,411,103	(2,411,103)	\$	3.94 -	\$	21.00	\$	7.36
Balances at December 31, 1997			\$	0.00 -	\$	15.00	\$	4.13
Grants of options Exercise of options and issuance	(834,750)	834,750	\$	2.25 -	\$	4.94	\$	3.40
of stock awards		(106.355)	^	0.00	Ċ	3.94	\$	0.42
		(186,355)					\$ \$	
Forfeitures	580,811 	(580,811) 	Ş	0.00 -	Þ	15.00	Ş	4.05
Balances at December 31, 1998	819,836 ======	2,534,839 =======	\$	0.00 -	\$	11.90	\$	3.88

</TABLE>

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At December 31, 1998, options to purchase 1,063,984 shares of common stock were exercisable at a weighted average exercise price of \$4.50 per share. At December 31, 1997, options to purchase 350,279 shares of common stock were exercisable at a weighted average exercise price of \$4.67 per share.

Exercise prices for options outstanding as of December 31, 1998 ranged from \$0.23 to \$11.90 per share. The weighted average remaining contractual life of those options is 8.6 years.

<TABLE> <CAPTION>

				Weighted- Stock awards Weighted- average Number Weighted-					rhtad-		
E	Exercise price range			and stock options outstanding	av exe	erage ercise erice	remaining contractual life (in years)		of exercisable options	average exercise price	
<s></s>				<c></c>	<c></c>		<c></c>		<c></c>	<c></c>	
\$	0.00	\$	2.60	173,233	\$	0.95		8.4	21,899	\$	0.35
\$	2.61	\$	5.20	2,236,233	\$	3.80		8.7	916,712	\$	3.94
\$	5.21	\$	11.90	125,373	\$	9.33		6.6	125,373	\$	9.33
				2,534,839	\$	3.88		8.6	1,063,984	\$	4.50
			==========					=========	====	=========	

</TABLE>

On October 29, 1997, the Board of Directors approved a resolution to offer eligible employees, including executive officers, holding stock options granted under the Plan, the opportunity to exchange their existing stock options for new options at the then current fair market value of \$3.94 per share. The resolution maintains the same vesting schedule for unvested shares as was applicable for the existing stock options, but increases the service period for those shares previously vested. Vested existing options exchanged for the new options will vest 50% after six months and 50% after one year.

The Company applies APB 25, "Accounting for Stock Issued to Employees." Pro forma information regarding net loss per share is required by SFAS 123, "Accounting for Stock-Based Compensation," and has been determined as if the Company had accounted for its employee and director stock options under the fair value method described in that Statement. The Black-Scholes option pricing model is used to calculate the fair value of these options for 1996, 1997, and 1998 with the following assumptions: dividend yield of zero % for all three years, volatility factors of 0.66 for 1996, 0.57 for 1997, and 0.74 for 1998, risk-free interest rate of 6.2% for 1996 and 1997 and 6.1% for 1998, assumed forfeiture rate of 6.4% for 1996, 10.57% for 1997 and 1998, and an expected life of 4.0 years for all three years.

The Black-Scholes options valuation model was developed for use in estimating the fair value of traded options which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options. However, the Company has presented the pro forma net loss and pro forma basic and diluted net loss per common share using the assumptions noted above.

Had compensation costs for the Company's stock option plans been determined based upon the fair value at the grant date for awards under these plans consistent with the methodology prescribed under SFAS 123, the Company's net loss and net loss per share for 1996, 1997, and 1998 would have been as follows:

<TABLE> <CAPTION>

		For th	e Year	rs ended De	cember	31,
(IN THOUSANDS)		1996		1997	1	998
<\$>	<c></c>		<c></c>		<c></c>	
Net loss - as reported	\$	(29,643)	\$	(39,731)	\$	(21,349)
Net loss - pro forma	\$	(30,706)	\$	(41,006)	\$	(22,525)
Basic and diluted net loss per share - as reported	\$	(1.48)	\$	(1.85)	\$	(0.97)
Basic and diluted net loss per share - pro forma	\$	(1.53)	\$	(1.90)	\$	(1.02)

</TABLE>

The weighted average fair value of options granted at fair market value during 1996, 1997, and 1998, is estimated at \$5.73, \$2.23, and \$2.01, respectively on the date of grant. The weighted average of options granted at below fair market value during 1996 and 1997 is estimated at \$7.39 and \$2.19 respectively on the date of grant. No options were granted at below fair market value in 1998.

SFAS 123 is effective for options granted by the Company commencing January 1, 1995. All options granted before January 1, 1995 have not been valued and no pro forma compensation expense has been recognized. However, any option granted before January 1, 1995 that was repriced in 1996 is treated as a new grant within 1996 and valued accordingly. In addition, as compensation expense is recognized over the vesting period of the option, the pro forma effect will not be fully reflected until approximately 1999.

## 14. INCOME TAXES

As of December 31, 1998, the Company had federal and state net operating loss carryforwards of approximately \$165,400,000 and \$15,600,000, respectively. The Company also had federal research and development tax credit carryforwards of approximately \$3,800,000. The federal net operating loss and credit carryforwards will expire at various dates beginning in the year 2000 through 2018, if not utilized. The state of California net operating losses will expire at various dates beginning in 1999 through 2004, if not utilized.

Utilization of the Company's net operating loss carryforwards and credits may be subject to an annual limitation due to the "change in ownership" provisions of the Internal Revenue Code of 1986 and similar state provisions.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets for financial reporting and the amount used for income tax purposes. Significant components of the Company's deferred tax assets for federal and state income taxes for the years ended December 31, 1997, and 1998 are as follows:

<TABLE>

## (IN THOUSANDS)

At December 31,		1997		1998
<s></s>	<c></c>		<c></c>	
Deferred tax assets				
Net operating loss carryforwards	\$	48,600	\$	57,100
Research credits		4,900		5,900
Capitalized research expenses		6,700		8,200
Other		3,300		1,500
Total deferred tax assets	\$	63 <b>,</b> 500	\$	72,700
Valuation allowance for deferred tax assets		(63,500)		(72,700)
Net deferred tax assets	\$		\$	
<td></td> <td></td> <td></td> <td></td>				

The net valuation allowance increased by \$17,800,000 and \$9,200,000 in 1997 and 1998, respectively.

## 15. RELATED PARTIES

During the years ended December 31, 1998, 1997, and 1996, legal fees of approximately \$244,000, \$2,816,200 and \$1,843,100, respectively, were paid to Brobeck, Phleger & Harrison, a law firm in which a current director of the Company is a senior partner. As of December 31, 1998 and 1997, amounts owed to Brobeck, Phleger, & Harrison were \$16,000 and \$111,800, respectively.

In 1997, a director of the Company received \$750,000 in exchange for promissory notes secured by a deed of trust. The notes were payable in 1998 and accrued interest at 7% per annum. In 1998, the director repaid \$346,000 of principal and accrued interest of \$4,000. The remaining balance of the loan was extended to September 22, 1999. During 1997, two officers received \$100,000 and \$500,000, respectively, in exchange for non-interest bearing promissory notes secured by deeds of trust. The loans are to be forgiven over a period of four to seven years from their inception. The compensation charge relating to the forgiveness in 1998 was not material.

In March 1997, the Board of Directors authorized a special risk sharing arrangement designated as the Shared Investment Program ("the Program"). Under the Program, the Company's executive officers and other key managerial personnel were given the opportunity to purchase shares of Common Stock in an individually designated amount per participant determined by the Committee of the Board of Directors. A total of 370,000 shares were purchased under the

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Program by nine eligible employees at \$6.25 per share, the fair market value of the Common Stock on June 25, 1997, for an aggregate consideration of \$2,312,500.

#### 16. EMPLOYEE SAVINGS AND RETIREMENT PLAN

The Company adopted a 401 (k) savings and retirement plan in January 1990. The plan covers all eligible employees who are 21 years of age or older. In May 1996, the Board of Directors approved a matching contribution under the Company's 401 (k) plan. Under this program, retroactive to January 1, 1996, the Company made a matching contribution on behalf of each eligible employee equal to 12.5% of salary deferral contribution for 1996 and 50% beginning on January 1, 1997. At the end of each quarter, the Company issues new shares of its common stock, using the fair market value, for its matching contribution. Company matching contributions were \$71,000, \$424,000 and \$379,000 in 1996, 1997 and 1998, respectively.

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#### REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

The Board of Directors and Stockholders Matrix Pharmaceutical, Inc.

We have audited the accompanying consolidated balance sheets of Matrix Pharmaceutical, Inc. (a development stage company) as of December 31, 1997 and 1998, and the related consolidated statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 1998 and for the period from inception (February 11, 1985) to December 31, 1998. 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 generally accepted auditing standards. 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 consolidated financial position of Matrix Pharmaceutical, Inc. (a development stage company) at December 31, 1997 and 1998, and the consolidated results of its operations and cash flows for each of the three years in the period ended December 31, 1998 and for the period from inception (February 11, 1985) to December 31, 1998, in conformity with generally accepted accounting principles.

ERNST & YOUNG LLP

Palo Alto, California January 25, 1999

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## EXHIBIT 23.1

## CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-32213) pertaining to the 1988 Restricted Stock Plan and the 1991 Directors' Stock Option Plan of Matrix Pharmaceutical, Inc., of our report dated January 25, 1999, with respect to the consolidated financial statements of Matrix Pharmaceutical, Inc. included in the Annual Report (Form 10-K) for the year ended December 31, 1998.

Palo Alto, California March 25, 1999

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