GENETRONICS BIOMEDICAL CORP
Form 10-K405/A
February 25, 2002

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

FORM 10-K/A
Amendment No. 2 to Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF
THE SECURITIES EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED MARCH 31, 2001

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

COMMISSION FILE NO. 0-29608
GENETRONICS BIOMEDICAL CORPORATION
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

Delaware	33-0969592
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
11199 SORRENTO VALLEY ROAD SAN DIEGO, CALIFORNIA (Address of principal executive offices)	92121-1334 (Zip Code)

REGISTRANT S TELEPHONE NUMBER, INCLUDING AREA CODE: (858) 597-6006

SECURITIES REGISTERED PURSUANT TO SECTION 12(B) OF THE ACT: NONE

SECURITIES REGISTERED PURSUANT TO SECTION 12(G) OF THE ACT:

COMMON STOCK, $0.001 PAR VALUE

(Title of Class)

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

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

The number of shares outstanding of the Registrant s Common Stock, which at the time of the original 10-K filing had no par value, was 33,756,718 as of May 10, 2001. The aggregate market value of the voting stock (which consists solely of shares of Common Stock) held by non-affiliates of the Company as of May 10, 2001 was approximately $43,999,300 based on $1.48 per share, the closing price on that date of Common Stock on the American Stock Exchange. *

* Excludes 4,027,461 shares of Common Stock held by directors and officers, and shareholders whose beneficial ownership exceeds 10% of the shares outstanding on May 10, 2001. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Company, or that such person is controlled by or under common control with the Company.

DOCUMENTS INCORPORATED BY REFERENCE

Certain exhibits filed with the Registrant s prior registration statements, Forms 10-K, 10-Q, and 8-K are incorporated herein by reference into Part IV of this report.

EXPLANATORY NOTE

This Amendment No. 2 on Form 10-K/A is filed by Genetronics Biomedical Corporation (formerly known as Genetronics Biomedical Ltd.) as an amendment to its Annual Report on Form 10-K for the fiscal year ended March 31, 2001 to amend and restate in their entirety Items 1, 6, 7, and the financial statements included in Item 14 (a) (including the notes thereto), so that such sections are presented in accordance with the generally accepted accounting principles in the United States. Such sections had been previously presented in accordance with the generally accepted accounting principles in Canada. Unless otherwise noted or indicated by context, all statements in this Amendment are made as of March 31, 2001.

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ITEM 1. BUSINESS

OVERVIEW

We were incorporated in British Columbia, Canada on August 8, 1979 under the name of Concord Energy Corp. We changed our name to United Safety Technology Inc. on February 17, 1988, to Consolidated United Safety Technology Inc. on January 3, 1990, and then to Genetronics Biomedical Ltd., on September 29, 1994. On June 15, 2001, the Company completed a change in its jurisdiction of incorporation from British Columbia, Canada into the state of Delaware. The change was accomplished through a continuation of Genetronics Biomedical Ltd., a British Columbia Corporation, into Genetronics Biomedical Corporation, a Delaware corporation. We carry on our business through our operating subsidiary Genetronics, Inc., a California corporation. Genetronics, Inc. was incorporated in California on June 29, 1983. Genetronics, Inc. had a subsidiary called Genetronics S.A., which was incorporated in France on January 30, 1998. Genetronics S.A. was formed primarily to manage clinical trials that were being conducted in France. Effective May 2000, the Company closed the operations of Genetronics S.A. and subsequently sold its investment for nominal consideration to Geser S.A., a company owned by Genetronics S.A. s former General Manager. All of our business activities are conducted through Genetronics, Inc. Unless otherwise indicated, all references to Genetronics or the Company refer to Genetronics Biomedical Corporation and Genetronics, Inc. on a consolidated basis.

The Company s originally filed Form 10-K included consolidated financial statements for the year ended March 31, 2001 prepared in accordance with Canadian generally accepted accounting principles. As a result of the change in its jurisdiction of incorporation, the Company is filing this amendment to Form 10-K whereby its consolidated financial statements will be presented in accordance with U.S. GAAP. In addition, selected Consolidated Financial Data and Management s Discussion and Analysis have been modified to address the results of operations as presented in accordance with U.S. GAAP.

We are a San Diego-based drug and gene delivery company specializing in developing technology and hardware focused on electroporation. Electroporation is the application of brief, controlled pulsed electric fields to cells, which cause tiny pores to temporarily open in the cell membrane. Immediately after electroporation, the cell membrane is more permeable to drugs and other agents. In the lab, researchers use electroporation to introduce genes, drugs, and other compounds into cells and experimental animals. This is a common and well-known procedure and more than 4,000 scientific papers have been published describing results achieved using electroporation.

While widely used in the research arena, electroporation is a relatively new technology in the therapeutic arena. One of the major difficulties in many forms of drug or gene therapy is that the pharmaceutical agent or gene is often not able to penetrate the relatively impermeable walls of cells. The pores produced by electroporation permit entry of such agents into cells to a much greater extent than if the drug or gene was administered without electroporation. When electroporation is used in conjunction with drugs, genes, or other therapeutic agents, it is referred to as Electroporation Therapy (EPT). We operate through our two divisions: (i) the Drug and Gene Delivery Division, through which we are developing drug and gene delivery systems based on electroporation to be used in the treatment of disease and, (ii) the BTX Instrument Division, which develops, manufactures, and sells electroporation equipment to the research laboratory market for in vitro and for in vivo animal experimentation.

The Drug and Gene Delivery Division focuses on the development of human-use equipment that is designed to allow physicians to use EPT to achieve more efficient and cost-effective delivery of drugs or genes to patients with a variety of illnesses, including cancer. Our proprietary electroporation drug and gene delivery system, the Genetronics MedPulser® system, has been used with bleomycin, a chemotherapeutic agent, in clinical trials conducted in the United States, Australia, Europe and Canada for treatment of head and neck cancer, as well as melanoma, liver, pancreatic, basal cell and Kaposi sarcoma cancers.

DRUG AND GENE DELIVERY DIVISION

OVERVIEW

Through our Drug and Gene Delivery Division, we are developing drug and gene delivery systems based on the technology of electroporation to be used in combination with drugs or genes in the treatment of disease. There are many diseases where improved drug delivery is important. Our Drug and Gene Delivery Division has identified five potential areas of application for our electroporation technology oncology, gene therapy, dermatology, cardiology and transdermal drug delivery. At present, the primary areas of our focus are oncology and gene therapy.

Our Drug and Gene Delivery Division s most advanced product candidates treat solid malignant tumors such as squamous cell carcinoma, melanoma, and adenocarcinoma in the areas of application of oncology and dermatology. We have completed Phase II clinical trials in the United States of EPT and bleomycin in the treatment of head and neck cancer and melanoma. Initial results from the clinical trials carried out in Europe have allowed us to obtain a CE Mark certification qualifying the MedPulser® system for sale in Europe with respect to the treatment of

head and neck cancer and melanoma using EPT and bleomycin. We intend to initiate the marketing of the MedPulser® System in Europe in 2001.

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We intend to develop and pursue other appropriate targets using the MedPulser® System to deliver bleomycin or other chemotherapeutic agents. Such studies will begin as Phase I or Phase II clinical trials. Phase I clinical trials are early stage trials in human subjects, used to test a drug or delivery system for safety. Phase II clinical trials assess the effectiveness of a treatment, as well as adding to safety data. Phase III clinical trials evaluate the comparative safety and efficacy of a drug or delivery system and the data from these trials are used by regulatory agencies to approve or reject a product licensing application.

Our drug delivery system, including the MedPulser® instrument and the disposable applicators, are subject to various regulatory requirements depending on the country of sale. The Drug and Gene Delivery Division MedPulser® system has been awarded ISO 9001, EN46001 and ISO 13485 registration, as well as CE mark certification in Europe.

MARKET

Our Drug and Gene Delivery Division is expected to enter the commercial market with equipment to be used in the treatment of cancer (oncology). Cancer is a life threatening disease affecting millions of people worldwide. The World Health Organization reports that cancer will remain one of the leading causes of death worldwide for years to come. In the United States, approximately 13 million new cases were diagnosed between 1990 and 1999. To further illustrate the market potential for EPT, solid tumor cancers, the first target for EPT, constitute the majority of all cancers. The majority of cancer victims are over age 65 and are supported by government-funded programs. In the United States the costs of cancer, including mortality, morbidity and direct medical costs, exceed $107 billion per year: some $37 billion for direct medical costs (total of all health expenditures); at least $11 billion for indirect morbidity costs (cost of lost productivity due to illness); and over $59 billion for indirect mortality costs.

There is still very much that scientists do not know about cancer; consequently, there are significant unmet needs in the treatment of cancer. The oncology business unit within the Drug and Gene Delivery Division has initially targeted those indications for which current treatment modalities result in a poor quality of life and very high mortality rates. Specialized applicators are being designed which will allow EPT to treat other solid tumor cancers with minimally invasive procedures.

In the United States, the cumulative dollar value of treatments and technologies commonly used in the curative and palliative management of cancer exceeded $8 billion in 1999 and is expected to continue growing at a rate of approximately 12% annually. Our analyses project that EPT could be applicable to over 4,000,000 cancer patients. This analysis is based upon the reported incidence of head and neck cancers throughout the world as reflected by statistics obtained from the American Cancer Society, the World Health Organization and the National Institutes of Health.

TREATMENT OF TUMORS

Equipment made by our BTX Instrument Division has been used by our investigators and in other laboratories to screen drugs for their effectiveness in killing tumor cells in test tubes and to study the drugs mode of action. Our scientists, and outside researchers, also have studied the combination of electroporation and various agents to destroy tumors in animals and humans.

In most of the clinical protocols, the site of the tumor is anesthetized and the chemotherapeutic agent of choice (bleomycin) is injected directly into the tumor. The therapeutic agent is allowed to diffuse throughout the tumor, which can take one to several minutes depending on the size, type and location of the tumor. Once the drug is distributed in the tumor, the electrical field is applied by the MedPulser® system so as to create a greater permeability in the cells walls to allow the chemotherapeutic agent to enter the cells.

The entire procedure can be completed in 20 minutes or less and typically needs to be done only once. The dosage of drug used in the published results is based on tumor volume, and is typically a small fraction (1/3 to as little as 1/50) of the dosage that would be used systemically. As a result of the lower dosage administered locally, side effects have been minimal. Tumor death with sloughing and ulceration were common reactions following EPT. No episodes of injury to normal (non-tumor) tissue adjacent to the tumors have been observed.

MEDPULSER® SYSTEM

The MedPulser® system is an electroporation system designed for the clinical application of EPT. The technology is intended to treat various malignant and non-malignant tumors by locally applying a controlled electric field to targeted tumor tissues previously injected with a chemotherapeutic agent. The controlled short duration electric field pulses temporarily increase the cellular membrane permeability of the tumor cell membrane allowing the therapeutic agent to more easily enter the tumor cells and kill them.

The system has two components: (1) a medical instrument which creates the electric field (the MedPulser® instrument); and (2) a single use, sterile, disposable electrode applicator. The electrodes may be needles, plates, or other configurations, depending on the geometry of the tumor

and its location.

The instrument was designed for ease of use, such that minimal user input is needed to apply the therapy. Based on the size and anatomical location of the tumor to be treated, a physician selects the most appropriate electrode applicator. The chosen applicator is then connected to the MedPulser® instrument,

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and it is the connection of applicator to instrument that automatically configures the therapy parameters for that particular applicator size and shape. Currently, several different electrode applicator configurations are available. The applicators vary in needle length, needle gauge, electrode needle spacing, tip angle and handle configuration so as to allow the physician to access a greater range of tumors.

New models of electrode applicators will be considered in the future to address customer needs. The system is designed such that the installed base of MedPulser® generator instruments allows for a wide variety of new electrode applicator configurations. Also, the system incorporates other features to minimize the possibility of applicator reuse as well as prevent the use of competitive applicators with the MedPulser® instrument. The commercial version MedPulser® system has been certified by an independent test laboratory as meeting strict international product standards. Our drug delivery device, including the MedPulser® system and the disposable electrode applicators, are subject to various regulatory requirements, depending on the country of sale.

In the United States, EPT utilizing the MedPulser® system and bleomycin drug is currently regulated as a combination drug-device system. We will be required to obtain both drug labelling and device approvals from the United States Food and Drug Administration (FDA). Clinical trials (Phase I, II and III) to support drug indication labelling require filing an Investigational New Drug Application (IND), followed by submission of a United States New Drug Application, and submission of a device Pre-Market Approval or 510(k), for marketing approval.

In most of the rest of the world, we anticipate that the MedPulser® system will be regulated as a device. In Europe, the device comes under the Medical Device Directive 93/42/EEC (MDD) and marketing requires CE mark certification of conformity to the quality system, production and clinical investigation essential requirements of the directive. We have obtained CE mark certification for electroporation devices, which allows us to sell and use the MedPulser® electroporation system for the treatment of solid tumors with bleomycin in Europe.

MEDICAL DEVICE MANUFACTURING

Our Drug and Gene Delivery Division must comply with a variety of regulations to manufacture our products for sale around the world. In Europe, we must comply with MDD. Our Drug and Gene Delivery Division has demonstrated the quality system is in place by securing ISO 9001 approval. It demonstrated compliance with international medical device standards with EN 46001 and ISO 13485 recognition. These all occurred in January 1999. In March 1999, the CE Mark was obtained for the MedPulser® electroporation system. To sell in the United States, we will need to be in compliance with FDA current Good Manufacturing Practices (GMP).

We employ modern manufacturing practices, which include outsourcing of significant custom assemblies used in the manufacture of the MedPulser® instrument. The instrument final assembly, testing and quality control functions are performed in a physically distinct area of the company where the appropriate controls are employed. We outsource the manufacture of the disposable electrode applicators to a GMP/ISO9002 compliant contract manufacturer.

CLINICAL STUDIES

North America Trials

In late 1997 the FDA gave us clearance to initiate multi-center Phase II clinical trials in the United States utilizing the MedPulser® electroporation system in combination with intralesional bleomycin to treat squamous cell carcinoma of the head and neck in patients who failed conventional therapies. We obtained IND clearance from the Canadian Health Protection Branch to initiate similar clinical trials in Canada. Two protocols were initiated. One cross-over-controlled study evaluated the effectiveness of the bleomycin-EPT treatment in tumors that failed an initial bleomycin-alone treatment. The second study was a single arm study that evaluated the effect of the bleomycin-EPT treatment as an initial therapy of the study tumors.

Twenty-five patients were enrolled in the controlled study and 25 patients were enrolled into the single arm bleomycin-EPT trial. The results based on the primary endpoint for response (50% or greater reduction in tumor size) are provided in the table below.

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Clinical Trial	Patients	Tumors	Clinical Response(1) (2) (3)	
			Responding Tumors	Non-Responding Tumors
North America Phase I/II	8	8	6(75%)	2(25%)
North America Phase II 25 37 1(3%) 36(97%) 01 Study Bleomycin only				
North America Phase II 17 20 11(55%) 9(45%) 01 Study				
North America Phase II 25 31 18(58%) 13(42%) 02 Study				
European Study 12 18 10(56%) 8(44%)				

(1) A clinical response is a clinically significant measurable result which is obtained on the basis of a defined course of treatment.
(2) Four tumors could not be evaluated(3) Control Group patients received only drug, no electric field

The two Phase II protocols involved a total of 42 tumors treated with bleomycin and EPT. Tumors treated in the trial include squamous cell carcinoma of the face, oral cavity, pharynx, larynx and sinus. The size of tumors treated ranged from less than one cubic centimeter to more than 132 cubic centimeters. In the crossover controlled Phase II study, patients initially received only the drug. Patients who did not respond to the drug alone were then treated with the complete system of drug and electric field. Of the 37 tumors on 25 patients treated only with the drug, only one demonstrated a clinical response. Seventeen of these patients, having 20 lesions, were subsequently treated with bleomycin and EPT and 55% achieved a clinical response. In the open-label Phase II study, all patients received full EPT as their initial treatment. Among the 25 patients (31 tumors) so treated, 58% achieved a clinical response.

A limited, well-controlled Phase III trial for palliative treatment of head and neck cancer in patients who failed conventional therapy may be sufficient to support NDA submission for this indication. Treatment of other diseases will involve expanded Phase II and Phase III trials pending successful outcome of the initial Phase I/II studies.

International Trials

In late 1997 and early 1998, we received ethics committee approval from multiple Consulting Committees for the Protection of Humans in Biomedical Research (CCPPRB) to initiate clinical trials in France in patients with pancreatic cancer, metastatic cancer in the liver, head and neck cancer, melanoma and Kaposi s sarcoma. There were a total of 46 patients enrolled in these trials. CCPPRB provides oversight of proposed and actual human clinical trials to protect the participants in these trials and ensure that safety standards are met. These trials were initiated to demonstrate the MedPulser® system device s safety and performance in treating a variety of solid tumors in support of CE mark certification in accordance with the essential requirements of the Medical Device Directive (MDD). Results from those patients in this trial with head and neck cancer are reported under North America Trials above. We achieved CE mark certification in March 1999 from notified body TUV Product Service GMBH (TUV). TUV oversees and audits clinical trials, reviews the results of the these trials and certifies compliance with established European standards. The CE mark certification allows us to market our MedPulser® device within the EU member countries.

Current Developments

On October 6, 1998, we entered into a comprehensive License and Development Agreement and a Supply Agreement with Ethicon, Inc., a Johnson & Johnson company, involving our proprietary drug delivery system for EPT treatment of cancer. In August 5, 1999, these agreements were assigned to Ethicon Endo-Surgery, Inc., another Johnson & Johnson company. Ethicon, Inc. and Ethicon Endo-Surgery, Inc. are referred to as Ethicon in this filing. On July 26, 2000, we received written notice from Ethicon Endo-Surgery, Inc. that it had elected to exercise its discretionary right to terminate, without cause, the License and Development Agreement and the Supply Agreement. All rights for the development and distribution of Genetronics proprietary electroporation drug delivery system for the treatment of cancer were returned to Genetronics on termination of the agreement on January 2001.

In September 2000, we executed an exclusive license agreement with the University of South Florida Research Foundation, Inc. (USF) that granted to us the worldwide license to USF s rights in certain patents and patent applications generally related to needle electrodes. Genetronics and USF jointly developed these electrodes. The needle electrodes are components of Genetronics electroporations systems and are used to deliver electric pulses to cells and tissues during the process of electroporation. Pulsed electric fields generated during the electroporation process cause a temporary but significant increase in the permeability of human cells. This makes it easier for drugs and genes to enter cells, a key element for successful cancer or gene therapy treatment. In April 2001, we initiated a limited release of the MedPulser® Electroporation Therapy System, to key head and neck surgeons in several countries through a European Access Program (EAP). We have initiated a marketing evaluation of the technology, under the EAP, with a select group of

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thought leaders at premier cancer centers in Austria, the United Kingdom, Germany, the Netherlands, Switzerland, and the Czech Republic. Genetronics has a CE Mark certification qualifying the MedPulser® system for sale in Europe for the treatment of solid tumors. The lead indication for the planned launch of the MedPulser® Electroporation Therapy System is the treatment of head and neck cancers and the initiation of the EAP represents the beginning of the commercialization phase of our EPT program for head and neck cancer in Europe. We believe we have sufficient current resources to initiate a variety of activities directed toward the MedPulser® system launch and marketing in Europe, and for initiation of a Phase III clinical study in the United States. In April 2001, we completed a review of our existing clinical and regulatory information related to the Electroporation Drug Delivery System and submitted the results of this review to the FDA. The responses are described above under Clinical Studies North America Trials. The response rate determined pursuant to the review is consistent with previous data disclosed by us.

Research and Development Summary

We perform an ongoing review of our patent portfolio to confirm that our technologies are adequately protected. Each year we review our patent portfolio and write-off all abandoned patents.

Our Drug and Gene Delivery Division has, in the past, focused its research primarily in the areas of oncology, gene therapy, vascular therapy, transdermal delivery and dermatology. At present, the primary areas of focus are oncology and gene therapy.

The following table summarizes the programs of the Drug and Gene Delivery Division, the primary indications for each product and the current status of development. Developmental means the program is at the planning stage, protocols are being developed, and little if any animal work has commenced. Preclinical data means the program is at the stage where results from animal studies have been obtained. Clinical Trials means that human data is available. Tolerance study means a pilot clinical study to determine patient tolerance of electrical pulses at therapeutic dose.

Summary Table

		Stage of Approval	
Programs	**Development Status**	**United States & Canada**	**Europe**
DERMATOLOGY Basal Cell Cancer Clinical Trials Two pilot studies completed N/AGenital Warts Developmental N/A N/AONCOLOGY Head and Neck Cancer Clinical Trials Phase II Clinical Trials CE Mark and ISO 9001 ReceivedMelanoma Clinical Trials N/A CE Mark and ISO 9001 ReceivedMetastatic Liver Cancer Clinical Trials N/A CE Mark and ISO 9001 ReceivedPeripheral Sarcoma Preclinical data N/A CE Mark and ISO 9001 ReceivedBreast Cancer Preclinical data N/A CE Mark and ISO 9001 ReceivedProstate Cancer Preclinical data N/A CE Mark and ISO 9001 ReceivedGlioma Preclinical data N/A CE Mark and ISO 9001 ReceivedGENE THERAPY In vivo Gene Transfer blood protein encoding genes Preclinical data N/A N/AIn vivo Gene Transfer DNA vaccines Preclinical data N/A N/AIn vivo Gene Transfer anti-inflammatory protein encoding genes Preclinical data N/A N/AIn vivo Gene Transfer			

vascular protein encoding genes Preclinical data N/A N/AVASCULAR THERAPY Coronary Artery Disease, Marker genes & drugs Preclinical data N/A N/AVascular Disease, Heparin delivery (anti-restenosis) Preclinical data N/A N/ATRANSDERMAL DELIVERY PGE-1 delivery for Erectile dysfunction Tolerance Study One Device Tolerance Study completed N/ACalcitonin (osteoporosis) Preclinical data N/A N/AVitamin C Preclinical data N/A N/A

N/A means not applicable.

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GENE THERAPY

Gene therapy, in classical terms, involves the introduction of new genetic information into cells (transfection) for therapeutic purposes. Somatic cells of the body are transfected with a specific functioning gene to compensate for a genetic defect that results in a deficiency of a specific protein factor. In this context, one goal of gene therapy is to convert target cells or tissues into protein factories for the production and secretion of a normal protein locally or into the circulation. Many vexing genetic illnesses, including those currently treated by regular injection of a missing protein, can potentially be cured by supplying the functional gene to a sufficient number of cells under conditions which allow these cells to produce a therapeutically effective dose of the gene product.

Currently, single-gene recessive genetic disorders are the most accessible targets for correction by gene therapy, but ultimately polygenic and acquired diseases can and will be treated by using genes as pharmaceutical agents. In principle, any aspect of metabolism can be manipulated by modifying gene function, and it is this application of gene therapy that has enormous potential, extending far beyond the treatment of rare genetic diseases. For example, the ability to influence cellular metabolism by introducing specific genes has led to extensive investigation into the use of gene therapy for cancer treatment. By adding a tumor suppressor gene to certain types of cancers, the uncontrolled growth of those cells potentially could be brought under normal regulation. Likewise, transfecting tumor cells with genes capable of inducing programmed cell death can result in tumor ablation.

The methods of introducing genes have two specific approaches. Gene therapy can be performed either ex vivo or in vivo. Ex vivo gene therapy is the transfection of cells outside the body. Typically, a small amount of tissue is removed from the patient and the cells within that tissue are put into culture. The genetically modified cells, typically blood, bone marrow or others, are then returned to the patient, usually by blood transfusion or direct engraftment. In vivo gene therapy is the introduction of genetic information directly into cells in the patient s body. Theoretically, any tissue or cell type in the body can be used, and the choice is dependent on the specific goals of treatment and indications being treated. For internal tissue targets, a gene may be transfused through the blood stream to the organ or site of action, or it may be injected at the desired site, which is then electroporated to allow the gene to pass through the cell membrane.

Genes can also be applied topically or by injection to skin and then transferred into the cells of the skin by electroporation. Skin gene delivery by electroporation for gene therapy is currently being investigated at Genetronics as a safe, effective and cost-competitive approach. The skin is also a target for DNA vaccination. Vaccinating skin with DNA that encodes a specific antigen present in infectious agents or in tumor cells can produce beneficial immunological responses. Genes can also be used to directly fight cancer. The thymidine kinase gene, in conjunction with the prodrug ganciclovir, produces a potent antitumor effect based on drug toxicity and programmed cell killing via a bystander effect. Animal trials treating glioblastomas using this strategy have shown substantial success.

To make gene therapy a reality, many obstacles have to be overcome, including the safe, efficient delivery of the intact DNA construct into the host cells. The instrumentation we use for high-efficiency in vivo gene transfer is derived from the instrumentation developed for intratumoral and transdermal drug delivery. We believe electroporation will become the method of choice for DNA delivery to cells in many applications of gene therapy.

Because of the broad applicability of this technology, we have adopted the strategy of co-developing or licensing our technology exclusively or non-exclusively for specific genes or specific medical indications. In most cases, we contribute proprietary technology, expertise and instrumentation to optimize the delivery technology for particular applications. A partner company provides its proprietary DNA constructs, may conduct the pre-clinical research and clinical trials, and may introduce the new treatment and products to the marketplace. Genetronics and the partner company would share in the commercial success of the project. We have actively sought partners to develop this exciting technology to its full potential. On November 8, 1999, we entered into an 18-month research and option agreement with Boehringer Ingelheim International GmbH (Boehringer Ingelheim) related to the development of our electroporation technology for use in particular gene therapy applications. While the research results were successful Boehringer Ingelheim decided not to pursue that subject field and declined to exercise the option to license. On June 9, 2000, we announced that research studies using our electroporation systems were presented at a major international gene therapy conference. Additionally, in collaborations with Chiron Corporation and Valentis, Inc., our technology was shown to effectively deliver a variety of genes and DNA vaccines to skin and muscle of animals, including non-human primates.

BTX INSTRUMENT DIVISION

OVERVIEW

Our company, through our BTX Instrument Division, began developing and manufacturing electroporation equipment for the research laboratory market in 1983 and sold our first product in 1985. BTX was founded to develop and manufacture high quality scientific instrumentation that can be used by

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research scientists to perform various types of electroporation and electrofusion experiments. Electroporation in research is commonly used for transformation and transfection of all cell types, as well as for general molecular delivery at the cellular level. Electrofusion is the fusing together of two or more cells to form hybrid cells. Transformation is a process by which the genetic material carried by an individual cell is altered by incorporation of exogenous DNA into its genome. Transfection is the uptake, incorporation, and expression of exogenous DNA by eukaryotic cells.

The BTX Instrument Division is the second largest developer and marketer of electroporation instruments and supplies, with more than 2,000 customers in universities, companies, and research institutions worldwide. Our BTX Instrument Division sells its electroporation/electro cell fusion instrumentation and accessories to customers located in all states and territories of the United States and in over 47 foreign countries. The majority of our products are sold to customers in the United States, Europe and East Asia. The BTX Instrument Division currently produces an extensive line of electroporation instruments and accessories, including electroporation and electro cell fusion instruments, a monitoring device, and an assortment of electrodes and accessories.

PRODUCTS

BTX developed the square wave generator and graphic pulse analyzer for in vivo gene delivery and nuclear transfer research, fields that are rapidly increasing in scientific and medical interest. BTX also has developed a large volume flow-through electroporation system which offers an extensive collection of in situ and high throughput screening electroporation applicators.

BTX focused its efforts in recent years on product development and promotion of a new line of products for developing sophisticated applications. We released the ECM 830 in December 1998. It is a sophisticated square wave electroporation system with a menu driven digital user interface. In August 1999 we introduced the ECM 630, an Exponential Decay Wave Electroporation system that utilizes a Precision Pulse Technology, the new BTX Platform technology, and an all-new digital user interface. During the fiscal years ended March 31, 2001 and 2000, publications outlined the utilization of BTX equipment in newly developing animal in vivo gene delivery research. In the support of this research, we expanded our in vivo electrode offering and continue to emphasize the development of novel applicators.

The BTX Instrument Division s product line includes two exponential decay wave generators, one square wave generator, one electro cell fusion instrument and a graphic wave display monitor. In addition, this Division markets over 43 different types of electrodes and related accessories, as well as the standard disposable electroporation cuvettes, containers for holding liquid samples.

Exponential decay generators have been traditionally used for the electroporation of all cell types. Square wave generators have shown the greatest utility in the electroporation of mammalian and plant cells, as well as for animal in vivo applications. The Electro Cell Fusion System is used by researchers for embryo manipulation, hybridoma and quadroma formation, as well as for all cell fusion techniques, including applications involving adoptive immunotherapy.

While we, through our BTX Instrument Division, sell devices purportedly used by others for non-human embryo cloning, we do not ourself conduct embryo cloning. All of our BTX Instrument Division instruments sold to the research market carry the label not for human use. We are not aware of any regulations or industry guidelines limiting the use of our instrumentation in the animal research market. We comply with all National Institutes of Health guidelines on cloning and gene therapy. We also comply with all Federal and State regulations regarding the restrictions on research imposed on federally funded grants.

The BTX Instrument Division supplies three cuvette models, as do our competitors, plus some 43 additional specialized chambers electrodes, and accessories for electroporation. BTX in situ electrodes (e.g., Petri Pulser electrodes) position us to expand the electroporation market for adherent cell transfection applications, while high throughput screening electrodes and large volume production systems (e.g., 96-Well Coaxial Electrode, ElectroFlowPorator system), respectively, provide the BTX Instrument Division with an entry into the large volume and multi-sample processing arenas used by the major pharmaceutical and biotech companies conducting drug research.

The BTX Instrument Division meets regulatory requirements necessary to provide instrumentation to the research market for in vivo and in vitro animal experimentation. The BTX Instrument Division does not market equipment for use in humans, and, therefore, is not required to receive marketing approval from the FDA.

DISTRIBUTION

The main distributors of our BTX Instrument Division products in North America are VWR Scientific Products Corporation and Fisher Scientific Company, the two largest laboratory products suppliers in the United States. Both VWR and Fisher have over 250 representatives dedicated to the biological sciences in North America. Both VWR and Fisher have dedicated Life Science Programs in which BTX participates. The Fischer Scientific distribution agreement was signed in December 2000 and it is anticipated that they will become a main distributor in the

fiscal year ended March 31, 2002. In addition, the BTX Instrument Division distributes instruments and supplies through Intermountain Scientific Corporation, which has 20 field sales specialists in the United States. The BTX Instrument Division has over 45 international distributors in 47 countries, of which Merck Eurolab

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Holding GmbH is the biggest distributor in Europe. VWR Scientific Products Corporation and Merck Eurolab Holding GmbH are both members of the Merck Group. The BTX Instrument Division supports its distributors with advertising, exhibit exposure and lead generation.

ADVERTISING

The BTX Instrument Division advertises in major national and international scientific journals such as Science, Nature, Genetic Engineering News, and BioTechniques. The Division also attends and displays our products at about one scientific conference per month such as American Association for Cancer Research, American Society for Gene Therapy, and Neuroscience meeting. On a quarterly basis the BTX Instrument Division utilizes direct mail to an identified mailing list for specific product promotion. The BTX Instrument Division works closely with distribution partners in joint marketing campaigns and other value-added suppliers in co-marketing efforts.

COMPETITION

The main competitors of our BTX Instrument Division in the research marketplace are BioRad Laboratories, Eppendorf Scientific, Inc. and Hybaid Corporation. There are other companies entering and departing this market on a regular basis. The majority of these companies have other molecular biology product lines besides electroporation, while electroporation and electrofusion is the only business of the BTX Instrument Division. Most competing manufacturers concentrate on the exponential decay wave system and do not compete in the square wave market at this time. In the past 12 months, the competition in the marketing of electroporation cuvettes has increased, leading to the development of BTX-supplied private label products for both VWR and Fisher Scientific.

STRATEGIC PARTNERS

LICENSE AND DEVELOPMENT AGREEMENTS

On October 6, 1998, we entered into a comprehensive License and Development Agreement and a Supply Agreement with Ethicon, Inc., a Johnson & Johnson company, involving the use of our MedPulser® system for Electroporation Therapy in the treatment of solid tumor cancer. In addition, Johnson & Johnson Development Corporation purchased $6 million of shares of common stock of our company at a price of $2.68 per share, pursuant to the October 6, 1998 Stock Purchase Agreement. On August 5, 1999, we announced that Ethicon, Inc. had assigned the License and Development Agreement and Supply Agreement to Ethicon Endo-Surgery, Inc., another Johnson & Johnson company. On July 26, 2000, we received written notice from Ethicon Endo-Surgery, Inc. that it had elected to exercise its discretionary right to terminate, without cause, the License and Development Agreement and the Supply Agreement. As a result, all rights for the development and distribution of Genetronics proprietary electroporation drug delivery system for the treatment of cancer were returned to Genetronics in January 2001.

On September 20, 2000, the University of South Florida Research Foundation, Inc. (USF) granted to Genetronics, Inc. and Genetronics Biomedical Ltd. an exclusive, worldwide license to its rights in certain patents and patent applications generally related to needle electrodes. Genetronics and USF jointly developed these electrodes. The needle electrodes are components of Genetronics electroporation systems and are used to deliver electric pulses to cells and tissues during the process of electroporation. Pulsed electric fields generated during the electroporation process cause a temporary but significant increase in the permeability of human cells. This makes it easier for drugs and genes to enter cells, a key element for successful cancer or gene therapy treatment. The terms of the exclusive license include a royalty to be paid to USF based on net sales or products under the license. At March 31, 2001, no royalty had accrued as the Company had not yet generated any sales from this product. In addition, Genetronics has issued a total of 150,000 common shares and a total of 600,000 warrants of which 300,000 will vest subject to the achievement of certain milestones in Genetronics Biomedical Ltd. to USF and its designees, Drs. Heller, Jaroszeski, and Gilbert.

COLLABORATIVE RESEARCH AGREEMENTS

On November 8, 1999, we entered into an 18-month research and option agreement with Boehringer Ingelheim to develop our electroporation technology for use in a particular gene therapy application. Under the terms of the agreement, we will develop hardware and perform preclinical research relating to DNA delivery for cancer DNA vaccination. While the research results were successful Boehringer Ingelheim decided not to pursue that subject field and declined to exercise the option to license. On August 28, 2000, we announced that we had entered into a collaborative agreement with Johnson & Johnson Research Pty Ltd., a wholly owned subsidiary of Johnson & Johnson, located in Eveleigh, Australia, to explore the feasibility of using electroporation, Genetronics platform technology, to deliver nucleic acid materials into tumors in vivo.

Sales and Revenue

The following table provides the amount of net product sales, interest income, and revenue from grant funding and research and development agreements generated by us for the past three fiscal years. Segmented financial information is contained in 16 of the Consolidated Financial Statements that begin on Page F-1. The following table sets forth our selected consolidated financial data for the periods indicated, derived from consolidated financial statements prepared in accordance with accounting principles generally accepted in the United States.

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Period Ended:	March 31, 2001 12 months	March 31, 2000 12 months	March 31, 1999 12 months
PRODUCT SALES			
United States	$2,890,875	$2,905,065	$2,174,364
Rest of World	1,562,064	1,229,371	1,259,741
INTEREST INCOME			
United States	431,729	497,586	248,417
Canada	11,900	58,607	52,494
GRANT FUNDING			
United States	101,086	334,901	354,135
REVENUES UNDER COLLABORATIVE RESEARCH AND DEVELOPMENT ARRANGEMENTS			
Germany	411,616	91,335	0
United States	48,095	100,000	33,048
LICENSE FEE AND MILESTONE PAYMENTS			
United States	3,730,392	416,667	4,500,000

We, like many biomedical companies, devote a substantial portion of our annual budget to research and development. For the year ended March 31, 1999, research and development expenses totaled $8,086,959; for the year ended March 31, 2000, they totaled $6,977,220 and for the year ended March 31, 2001, they totaled $6,436,377. These amounts far exceed revenues from research arrangements and contribute substantially to our losses. We anticipate a reduction in losses when we market products developed by our Drug and Gene Delivery Division. The launch of the first such products in Europe is anticipated to be in 2001, and will most likely be followed by launch in the United States subject to FDA approval at a later date.

INTELLECTUAL PROPERTY

As of April 21, 2001, we had 36 issued United States patents and 48 issued and granted foreign patents. The duration of these patents are from ten to seventeen years. In addition, as of April 21, 2001 we had 3 allowed United States patent applications, an additional 18 pending United States applications, and additional pending foreign patent applications. We also license certain technologies in our business, the typical duration of these licenses range from ten to seventeen years.

We have registered on the Principal Register of the United States Patent and Trademark Office the following trademarks: BTX (Mark), BTX (Logo), ELECTRONIC GENETICS, MANIPULATOR, OPTIMIZOR, HUMAN IN SQUARE (Design), ENHANCER, and MEDPULSER. The following United States trademark applications are pending: COSMETRONICS and GENETRODES. We have registered the BTX and MEDPULSER trademarks in Canada, and have applied to trademark GENETRONICS in Canada. We have a European Community Trade Mark registration for GENETRONICS, BTX and for MEDPULSER. We have registered the MEDPULSER and BTX marks in Japan. We have registered the BTX mark in South Korea and have registered the GENETRONICS mark in the United Kingdom. We are not aware of any claims of infringement or other challenges to our right to use our marks.

EMPLOYEES

As of May 10, 2001, we employed 66 people on a full-time basis. Of the total, 21 were in product research and development, 10 in sales, marketing and support, 11 in manufacturing, and 24 in finance and administration. Our success is dependent on our ability to attract and retain qualified employees. Competition for employees is intense in the biomedical industry. None of our employees is subject to collective bargaining agreements.

CERTAIN RISK FACTORS RELATED TO THE COMPANY S BUSINESS

OUR BUSINESS MODEL MAY CHANGE AS OUR PRIORITIES AND OPPORTUNITIES CHANGE AND OUR BUSINESS MAY NEVER DEVELOP TO BE PROFITABLE OR SUSTAINABLE.

There are many programs that to us seem promising and that we could pursue. However, with limited resources, we may decide to change priorities and shift programs away from those that we had been pursuing, for the purpose of exploiting other aspects of our core technology of electroporation. The choices we may make will be dependent upon numerous factors, which we cannot predict. We cannot assure you that our business model, as it currently exists or as it may evolve, will enable us to become profitable or to sustain operations.

IF WE DO NOT SUCCESSFULLY COMMERCIALIZE PRODUCTS FROM OUR DRUG AND GENE DELIVERY DIVISION, THEN OUR BUSINESS WILL SUFFER.

Our Drug and Gene Delivery Division is in the early development stage and our success depends on the success of the technology being developed by the Drug and Gene Delivery Division. Although we have received various regulatory approvals that apply to Europe for our equipment for use in treating

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solid tumors, the products related to such regulatory approval have not yet been commercialized. In addition, we have not yet received any regulatory approvals to sell our clinical products in the United States and further clinical trials are still necessary before we can seek regulatory approval to sell our product in the United States for treating solid tumors. We cannot assure you that we will successfully develop any products. If we fail to develop or successfully commercialize any products, then our business will suffer.

UNPREDICTABILITY OF CONDUCTING PRE-CLINICAL AND CLINICAL TRIALS OF OUR HUMAN-USE EQUIPMENT.

Before any of our human-use equipment can be sold, the FDA, or applicable foreign regulatory authorities, must determine that the equipment meets specified criteria for use in the indications for which approval is requested. The FDA will make this determination based on the results from our pre-clinical testing and clinical trials.

Clinical trials are unpredictable. Results achieved in early stage clinical trials may not be repeated in later stage trials, or in trials with more patients. When early, positive results are not repeated in later stage trials, pharmaceutical and biotechnology companies have suffered significant setbacks. Not only are commercialization timelines pushed back, but some companies, particularly smaller biotechnology companies with limited cash reserves, have gone out of business after releasing news of unsuccessful clinical trial results.

If any of the following events arise during our clinical trials or data review, then we would expect this to have a serious negative effect on our company and your investment:

The delivery of drugs or other agents by electroporation may be found to be ineffective or to cause harmful side effects, including death;

Our clinical trials may take longer than anticipated, for any of a number of reasons including a scarcity of subjects that meet the physiological or pathological criteria for entry into the study, a scarcity of subjects that are willing to participate through to the end of the trial, or data and document review;

The reporting clinical data may change over time as a result of the continuing evaluation of patients or the current assembly or review of existing clinical and pre-clinical information;

Data from various sites participating in the clinical trials may be incomplete or unreliable, which could result in the need to repeat the trial or abandon the project; and

The FDA and other regulatory authorities may interpret our data differently than we do, which may delay or deny approval.

Clinical trials are generally quite expensive. A delay in our trials, for whatever reason, will probably require us to spend additional funds to keep the product(s) moving through the regulatory process. If we do not have or cannot raise the needed funds, then the testing of our human-use products could be shelved. In the event the clinical trials are not successful, we will have to determine whether to put more money into the program to address its deficiencies or whether to abandon the clinical development programs for the products in the tested indications. Loss of the human-use product line would be a significant setback for our company.

Because there are so many variables inherent in clinical trials, we cannot predict whether any of our future regulatory applications to conduct clinical trials will be approved by the FDA or other regulatory authorities, whether our clinical trials will commence or proceed as planned, and whether the trials will ultimately be deemed to be successful.

OUR BUSINESS IS HIGHLY DEPENDENT ON RECEIVING APPROVALS FROM VARIOUS UNITED STATES AND INTERNATIONAL GOVERNMENT AGENCIES AND CAN BE DRAMATICALLY AFFECTED IF APPROVAL TO MANUFACTURE AND SELL OUR HUMAN-USE EQUIPMENT IS NOT GRANTED.

The production and marketing of our human-use equipment and the ongoing research, development, preclinical testing, and clinical trial activities are subject to extensive regulation. Numerous governmental agencies in the U.S. and internationally, including the FDA, must review our applications and decide whether to grant approval. All of our human-use equipment must go through an approval process, in some instances for each indication in which we want to label it for use (such as, use for dermatology, use for transfer of a certain gene to a certain tissue, or use for administering a certain drug to a certain tumor type in a patient having certain characteristics). These regulatory processes are extensive and involve substantial costs and time.

Our company has limited experience in, and limited resources available for regulatory activities. Failure to comply with applicable regulations can, among other things, result in non-approval, suspensions of regulatory approvals, fines, product seizures and recalls, operating restrictions, injunctions and criminal prosecution.

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Any of the following events can occur and, if any did occur, any one could have a material adverse effect on us:

- There can be delays, sometimes long, in obtaining approval for our human-use devices;
- The rules and regulations governing human-use equipment such as ours can change during the review process, which can result in the need to spend time and money for further testing or review;
- If approval for commercialization is granted, it is possible the authorized use will be more limited than we believe is necessary for commercial success, or that approval may be conditioned on completion of further clinical trials or other activities; and
- Once granted, approval can be withdrawn, or limited, if previously unknown problems arise with our human-use product or data arising from its use.

WE RELY HEAVILY ON COLLABORATIVE AND LICENSING RELATIONSHIPS, AND WILL BE NEGATIVELY AFFECTED IF WE CANNOT MAINTAIN OR EXPAND EXISTING RELATIONSHIPS, AND INITIATE NEW ONES.

We rely and will continue to rely on partners and collaborators to fund some of our research and development expenses and to assist us in the research and development of our human-use equipment. Our largest partner had been Ethicon Endo-Surgery, Inc., a Johnson & Johnson company. On July 26, 2000, we received written notice from Ethicon Endo-Surgery, Inc. that it had elected to exercise its discretionary right to terminate, without cause, our License and Development Agreement and our Supply Agreement. If we are unable to enter into a relationship with a new partner for the Electroporation Drug Delivery System, our business could be adversely impacted. Moreover, loss of or any significant change in any of our material collaborative relationships could adversely impact our business.

Our clinical trials to date have used our equipment with the anti-cancer drug bleomycin. We do not currently intend to package bleomycin together with the equipment for sale, but if it should be necessary or desirable to do this, we would need a reliable source of the drug. In 1998, we signed a supply agreement with Abbott Laboratories under which Abbott would sell us bleomycin for inclusion in our package. If it becomes necessary or desirable to include bleomycin in our package, and this relationship with Abbott should be terminated, then we would have to form a relationship with another provider of this generic drug before any product could be launched.

We also rely on scientific collaborators at universities and companies to further our research and test our equipment. In most cases, we lend our equipment to a collaborator, teach him or her how to use it, and together design experiments to test the equipment in one of the collaborator s fields of expertise. We aim to secure agreements that restrict collaborators rights to use the equipment outside of the agreed upon research, and outline the rights each of us will have in any results or inventions arising from the work.

Nevertheless, there is always risk that:

- Our equipment will be used in ways we did not authorize, which can lead to liability and unwanted competition;
- We may determine that our technology has been improperly assigned to us or a collaborator may claim rights to certain of our technology, which may require us to pay license fees or milestone payments and, if commercial sales of the underlying product is achieved, royalties;
- We may lose rights to inventions made by our collaborators in the field of our business, which can lead to expensive legal fights and unwanted competition;
- Our collaborators may not keep our confidential information to themselves, which can lead to loss of our right to seek patent protection and loss of trade secrets, and expensive legal fights; and
- Collaborative associations can damage a company s reputation if they go awry and, thus, by association or otherwise, the scientific or medical community may develop a negative view of us.

We cannot guarantee that any of the results from these collaborations will be fruitful. We also cannot tell you that we will be able to continue to collaborate with individuals and institutions that will further our work, or that we will be able to do so under terms that are not too restrictive. If we are not able to maintain or develop new collaborative relationships, then it is likely the research pace will slow down and it will take longer to identify and commercialise new products, or new indications for our existing products.

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WE COULD BE SUBSTANTIALLY DAMAGED IF PHYSICIANS AND HOSPITALS PERFORMING OUR CLINICAL TRIALS DO NOT ADHERE TO PROTOCOLS OR PROMISES MADE IN CLINICAL TRIAL AGREEMENTS.

Our company also works and has worked with a number of hospitals to perform clinical trials, primarily in oncology. We depend on these hospitals to recruit patients for the trials, to perform the trials according to our protocols, and to report the results in a thorough, accurate and consistent fashion. Although we have agreements with these hospitals, which govern what each party is to do with respect to the protocol, patient safety, and avoidance of conflict of interest, there are risks that the terms of the contracts will not be followed.

For instance:

Risk of Deviations from Protocol. The hospitals or the physicians working at the hospitals may not perform the trial correctly. Deviations from protocol may make the clinical data not useful and the trial could be essentially worthless.

Risk of Improper Conflict of Interest. Physicians working on protocols may have an improper economic interest in our company, or other conflict of interest. When a physician has a personal stake in the success of the trial, such as can be inferred if the physician owns stock, or rights to purchase stock, of the trial sponsor, it can create suspicion that the trial results were improperly influenced by the physician s interest in economic gain. Not only can this put the clinical trial results at risk, but it can also do serious damage to a company s reputation.

Risks Involving Patient Safety and Consent. Physicians and hospitals may fail to secure formal written consent as instructed or report adverse effects that arise during the trial in the proper manner, which could put patients at unnecessary risk. This increases our liability, affects the data, and can damage our reputation.

If any of these events were to occur, then it could have a material adverse effect on our ability to receive regulatory authorization to sell our human-use equipment, not to mention on our reputation. Negative events that arise in the performance of clinical trials sponsored by biotechnology companies of our size and with limited cash reserves similar to ours have resulted in companies going out of business.

WE RELY HEAVILY ON OUR PATENTS AND PROPRIETARY RIGHTS TO ATTRACT PARTNERSHIPS AND MAINTAIN MARKET POSITION.

Another factor that will influence our success is the strength of our patent portfolio. Patents give the patent holder the right to keep others out of its patented territory. If someone practices within the patented territory of a patent holder, then the patent holder has the right to charge that person with infringement and begin legal proceedings, which can be lengthy and costly. We perform an ongoing review of our patent portfolio to confirm that our key technologies are adequately protected. If necessary, we may ask that one or more of our patents be re-examined or reissued by the United States patent office.

The patenting process, enforcement of issued patents, and defense against claims of infringement are inherently risky. Because our Drug and Gene Delivery Division relies heavily on patent protection, for us, the risks are significant and include the following:

Risk of Inadequate Patent Protection for Product. The United States or foreign patent offices may not grant patents of meaningful scope based on the applications we have already filed and those we intend to file. If we do not have patents that adequately protect our human-use equipment and indications for its use, then we will not be competitive.

Risk Important Patents Will Be Judged Invalid. Some of the issued patents we now own or license may be determined to be invalid. If we have to defend the validity of any of our patents, then it will require a lot of time and money to do so, and there is no guarantee of a successful outcome. In the event an important patent related to our drug delivery technology is found to be invalid, we may lose competitive position and may not be able to receive royalties for products covered in part or whole by that patent under license agreements.

Risk of Being Charged With Infringement. Although we try to avoid infringement, there is the risk that we will use a patented technology owned by another person and/or be charged with infringement. Defending against a charge of infringement can involve lengthy and costly legal actions, with no guarantee of a successful outcome. Biotechnology companies of roughly our size and financial position have gone out of business after fighting and losing an infringement battle. If we were prevented from using or selling our human-use equipment, then our business would be seriously affected.

Freedom to Operate Risks. We are aware that patents related to electrically assisted drug delivery have been granted to, and patent applications filed by, our potential competitors. We, along with some of our partners, have taken licenses to some of these patents, and will consider taking additional licenses in the future. Nevertheless, the competitive nature of our field of business and the fact that others

have sought patent protection for technologies similar to ours makes these significant risks.

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In addition to patents, we also rely on trade secrets and proprietary know-how. We try to protect this information with appropriate confidentiality and inventions agreements with our employees, scientific advisors, consultants, and collaborators. We cannot assure you that these agreements will not be breached, that we will be able to do much to protect ourselves if they are breached, or that our trade secrets will not otherwise become known or be independently discovered by competitors. If any of these events occurs, then we run the risk of losing control over valuable company information, which could negatively affect our competitive position.

WE RUN THE RISK THAT OUR TECHNOLOGY WILL BECOME OBSOLETE OR LOSE ITS COMPETITIVE ADVANTAGE.

The drug delivery business is very competitive, fast moving and intense, and expected to be increasingly so in the future. Other companies and research institutions are developing drug delivery systems that, if not similar in type to our systems, are designed to address the same patient or subject population. Therefore, we cannot promise you that our products will be the best, the safest, the first to market, or the most economical to make or use. If competitors products are better than ours, for whatever reason, then we will make less money from sales and our products risk becoming obsolete.

There are many reasons why a potential competitor might be more successful than us, including:

Superior Financial Resources. Some competitors have significantly more financial resources than we do. They can afford more technical and development setbacks than we can, and can devote more resources in an effort to improve development times or pursue alternate approaches.

Greater Experience. Some competitors have been in the drug delivery business longer than we have. They have greater experience than us in critical areas like clinical testing, obtaining regulatory approval, and sales and marketing. This experience or their name recognition may give them a competitive advantage over us.

Superior Patent Position. Some competitors may have a better patent position protecting their technology than we have or will have to protect our technology. If we cannot use our patents to prevent others from copying our technology or developing similar technology, or if we cannot obtain a critical license to another s patent that we need to make and use our equipment, then we would expect our competitive position to lessen.

Faster to Market. Some companies with competitive technologies may move through stages of development, approval, and marketing faster than us. If a competitor receives FDA approval before us, then it will be authorized to sell its products before we can sell ours. Because the first company to market often has a significant advantage over late-comers, a second place position could result in less than anticipated sales.

Reimbursement Allowed. In the United States, third party payers, such as Medicare, may reimburse physicians and hospitals for competitors products but not for our human-use products. This would significantly affect our ability to sell our human-use products in the United States and would have a serious effect on revenues and our business as a whole. Outside of the United States, reimbursement and funding policies vary widely.

OUR ABILITY TO ACHIEVE SIGNIFICANT REVENUE FROM SALES OR LEASES OF HUMAN-USE EQUIPMENT WILL DEPEND ON ESTABLISHING EFFECTIVE SALES, MARKETING AND DISTRIBUTION CAPABILITIES OR RELATIONSHIPS AND WE LACK SUBSTANTIAL EXPERIENCE IN THESE AREAS.

Our company has no experience in sales, marketing and distribution of clinical and human-use products. If we want to be direct distributors of the human-use products, then we must develop a marketing and sales force. This would involve a lot of money, training, and time. Alternatively, we may decide to rely on a company with a large distribution system and a large direct sales force to undertake the majority of these activities on our behalf. This route could result in less profit for us, but may permit us to reach market faster. In any event, we may not be able to undertake this effort on our own, or contract with another to do this at a reasonable cost. Regardless of the route we take, we may not be able to successfully commercialize any product.

WE HAVE OPERATED AT A LOSS AND WE EXPECT TO CONTINUE TO ACCUMULATE A DEFICIT; THERE IS A DOUBT ABOUT OUR ABILITY TO CONTINUE AS A "GOING CONCERN".

As of December 31, 2001, we had a deficit of $47,361,720. We have operated at a loss since 1994, and we expect this to continue for some time. The amount of our accumulated deficit will continue to grow, as it will be expensive to continue our clinical, research, and development efforts. If these activities are successful, and if we receive approval from the FDA to market human-use equipment, then even more money will be required to market and sell the equipment.

Most of the cash we have received during the fiscal year beginning April 1, 2001 came from the sale and distribution of special warrants in November of 2001 and sales of BTX research-use equipment. Other funds came from collaborative research arrangements, interest income on our investments and the exercise of stock options. We do not expect to receive enough money from these sources to completely pay for future activities. There is substantial doubt about our ability to continue as a going concern due to our historical negative cash flow and because we do not have access to sufficient committed capital to meet our projected operating needs for at least the next twelve months.

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WE WILL HAVE A NEED FOR SIGNIFICANT AMOUNTS OF MONEY IN THE FUTURE AND THERE IS NO GUARANTEE THAT WE WILL BE ABLE TO OBTAIN THE AMOUNTS WE NEED.

As discussed, we have operated at a loss, and expect that to continue for some time in the future. Our plans for continuing clinical trials, conducting research, furthering development and, eventually, marketing our human-use equipment will cost significant amounts of money. The extent of these costs will depend on many factors, including some of the following:

- The progress and breadth of preclinical testing and the size of our drug delivery programs, all of which directly influence cost;
- The costs involved in complying with the regulatory process to get our human-use products approved, including the number, size, and timing of necessary clinical trials and costs associated with the current assembly and review of existing clinical and pre-clinical information;
- The costs involved in patenting our technologies and defending them;
- Changes in our existing research and development relationships and our ability to enter into new agreements;
- The cost of manufacturing our human-use and research-use equipment; and
- Competition for our products and our ability, and that of our partners, to commercialize our products.

We plan to fund operations by several means. We will attempt to enter into contracts with partners that will fund either general operating expenses or specific programs or projects. Some funding also may be received through government grants. We cannot promise that we will enter into any such contracts or receive such grants, or, if we do, that our partners and the grants will provide enough money to meet our needs.

In the past, we have raised funds by public and private sale of our stock, and we may do this in the future to raise needed funds. Sale of our stock to new private or public investors usually results in existing stockholders becoming diluted . The greater the number of shares sold, the greater the dilution. A high degree of dilution can make it difficult for the price of our stock to rise rapidly, among other things. Dilution also lessens a stockholder s voting power.

We cannot assure you that we will be able to raise money needed to fund operations, or that we will be able to raise money under terms that are favorable to us.

IF WE DO NOT HAVE ENOUGH MONEY TO FUND OPERATIONS, THEN WE WILL HAVE TO CUT COSTS.

If we are not able to raise needed money under acceptable terms, then we will have to take measures to cut costs, such as: