

BIOTIME INC  
Form 10-K/A  
April 14, 2003

Items 6, 7, 7A, 8, and Exhibits 10.21, 23.1, 23.2, and 99.1 are filed herein pursuant to Rule 12b-25.

**SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM 10-K/A-1**

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

For the fiscal year ended December 31, 2002

OR

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

For the transition period from to

Commission file number 1-12830

**BioTime, Inc.**

(Exact name of registrant as specified in its charter)

California  
(State or other jurisdiction of  
incorporation or organization)

94-3127919  
(I.R.S. Employer  
Identification No.)

935 Pardee Street, Berkeley, California  
(Address of principal executive offices)

94710  
(Zip Code)

Registrant's telephone number, including area code (510) 845-9535

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

Common Shares, no par value  
(Title of Class)

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

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

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

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The approximate aggregate market value of voting stock held by nonaffiliates of the registrant was \$17,580,015 as of the last business day of the registrant's most recently completed second fiscal quarter. Shares held by each executive officer and director and by each person who beneficially owns more than 5% of the outstanding Common Shares have been excluded in that such persons may under certain circumstances be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

13,565,101

(Number of Common Shares outstanding as of March 20, 2003)

Documents Incorporated by Reference

None

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PART I

*Statements made in this Form 10-K that are not historical facts may constitute forward-looking statements that are subject to risks and uncertainties that could cause actual results to differ materially from those discussed. Words such as expects, may, will, anticipates, intends, plans, believes, seeks, estimates, and similar expressions identify forward-looking statements. See Risk Factors and Note 1 to Financial Statements.*

**Item 1. Description of Business**

**Overview**

BioTime, Inc. (the Company or BioTime ) is a development stage company engaged in the research and development of synthetic solutions that can be used as blood plasma volume expanders, blood replacement solutions during hypothermic (low temperature) surgery, and organ preservation solutions. Plasma volume expanders are used to treat blood loss in surgical or trauma patients until blood loss becomes so severe that a transfusion of packed red blood cells or other blood products is required. The Company is also developing a specially formulated hypothermic blood substitute solution that would have a similar function and would be used for the replacement of very large volumes of a patient's blood during cardiac surgery, neurosurgery and other surgeries that involve lowering the patient's body temperature to hypothermic levels.

The Company's first product, Hextend®, is a physiologically balanced blood plasma volume expander, for the treatment of hypovolemia. Hypovolemia is a condition caused by low blood volume, often from blood loss during surgery or from injury. Hextend maintains circulatory system fluid volume and blood pressure and keeps vital organs perfused during surgery. Hextend, approved for use in major surgery, is the only blood plasma volume expander that contains a medically approved form of starch called hetastarch, lactate, multiple electrolytes and glucose. Hextend is designed to compete with and to replace products that have been used to maintain fluid volume and blood pressure during surgery. These competing products include albumin and other colloid solutions, and crystalloid solutions. Albumin is a solution that contains a protein processed from human blood. Other colloid solutions contain proteins or a starch that keep the fluid in the patient's circulatory system in order to maintain blood pressure. Crystalloid solutions generally contain salts and may also contain other electrolytes, and are not as effective as Hextend, albumin and other colloids on a per unit basis in maintaining a patient's circulatory system fluid volume and pressure. Hextend is also completely sterile to avoid risk of infection. Health insurance reimbursements and HMO coverage now include the cost of Hextend used in surgical procedures.

Hextend is being sold in the United States by Abbott Laboratories under an exclusive license from the Company. Abbott also has the right to sell Hextend in Canada, where an application for marketing was approved on July 8, 2002. Hextend product launch in Canada is expected during the second quarter of this year. On March 27, 2003, the Company and CJ Corp. ( CJ ) entered into an Exclusive License Agreement (the CJ Agreement ) under which the Company granted to CJ an exclusive license to manufacture and sell Hextend and PentaLyte in the Republic of Korea. Abbott and CJ also have rights to obtain licenses to manufacture and sell other BioTime products. See Licensing for more information about the license granted to Abbott Laboratories and CJ.

As part of the marketing program, a number of studies have been conducted that show the advantages of receiving Hextend and other BioTime products during surgery. For example, the results of a clinical trial by NJ Wilkes et al performed in England and entitled "The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid-base and electrolyte status and gastric mucosal perfusion in elderly surgical patients" was published in the October 2001 edition of *Anesthesia and Analgesia*, and underscores a number of Hextend benefits including maintenance of normal acid-base balance, blood calcium and chloride levels and perfusion of portions of the gastro-intestinal tract. As future studies such as these are completed, the results will be presented at medical conferences and articles will be written for publication in medical journals. The Company is also aware of independent studies using Hextend that are being conducted which may be published in medical journals or reported at medical conferences. The outcome of future medical studies and timing of the publication or presentation of the results could have an effect on Hextend sales.

Hextend has been approved for use and added to hospital formularies, and has obtained or is seeking formulary committee approval at many additional hospitals. Inclusion on hospital formularies is important because it enables physicians to obtain Hextend without the need to special order it. Obtaining formulary approval generally takes several months and often requires diligent efforts.

The Company is also developing two other blood volume replacement products, PentaLyte,<sup>®</sup> and HetaCool,<sup>TM</sup> that, like Hextend,<sup>®</sup> have been formulated to maintain the patient's tissue and organ function by sustaining the patient's fluid volume and physiological balance.

Various colloid and crystalloid products are being marketed by other companies for use in maintaining patient fluid volume in surgery and trauma care, but those solutions do not contain the unique comprehensive combination of electrolytes, glucose, lactate and hydroxyethyl starch found in Hextend, PentaLyte, and HetaCool. The use of competing solutions can contribute to patient morbidity, including conditions such as hypovolemia, fluid accumulation in body tissues, impaired blood clotting, and a disturbance of the delicate chemical balances on which most of the body's chemical reactions depend. One of these competing products is 6% hetastarch in saline solution. On June 14, 2002, the Blood Products Advisory Committee of the United States Food and Drug Administration voted 8-0 with 2 abstentions to recommend to the FDA that the labeling of 6% hetastarch in saline should be changed by adding a warning regarding the risk of bleeding during cardiac surgery. No such recommendation was made for Hextend since it is a different product.

Another competing product is albumin produced from human plasma. Albumin is more expensive than Hextend and is subject to supply shortages. An FDA warning has cautioned physicians about the risk of administering albumin to seriously ill patients.

Based upon the results of its clinical studies and laboratory research, the Company has determined that in many emergency care and surgical applications it is not necessary for a plasma volume expander to include special oxygen carrying molecules to replace red blood cells. Therefore, the Company is developing formulations that do not use costly and potentially toxic oxygen carrying molecules such as synthetic hemoglobin and perfluorocarbons. However, recent laboratory findings

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by Company scientists suggest that Hextend can allow hemoglobin-based oxygen carrier solutions to be used more effectively.

In order to commence clinical trials for regulatory approval of new products, such as PentaLyte and HetaCool, or new therapeutic uses of Hextend, it will be necessary for the Company to prepare and file with the FDA an Investigational New Drug Application ( IND ) or an amendment to expand the present IND for additional Hextend studies. Filings with foreign regulatory agencies will be required to commence clinical trials overseas.

BioTime has completed a Phase I clinical trial of PentaLyte involving a small number of subjects and has submitted its findings to the FDA. BioTime plans to test PentaLyte for the treatment of hypovolemia in surgery. PentaLyte contains a lower molecular weight hydroxyethyl starch than Hextend, and is more quickly metabolized. PentaLyte is designed for use when short lasting volume expansion is desirable. BioTime's ability to commence and complete its clinical studies of PentaLyte depends on its cash resources and the costs involved, which are not presently determinable.

BioTime is also continuing to develop solutions for low temperature surgery and trauma care. A number of physicians have reported using Hextend to treat hypovolemia under mild hypothermic conditions during cardiac surgery. Additional cardiac surgeries have been performed at deeper hypothermic temperatures. In one case, Hextend was used to treat hypovolemia in a cancer patient operated on under deep hypothermic conditions in which the heart was arrested. Once a sufficient amount of data from successful low temperature surgery has been compiled, the Company plans to seek permission to conduct trials using Hextend as a complete replacement for blood under near-freezing conditions. BioTime currently plans to market Hextend for complete blood volume replacement at very low temperatures under the trade mark HetaCool after FDA approval is obtained.

The cost of preparing regulatory filings and conducting clinical trials is not presently determinable, but could be substantial. It will be necessary for the Company to obtain additional funds in order to complete any clinical trials that it may conduct for its new products or for new uses of Hextend.

In addition to developing clinical trial programs, the Company plans to continue to provide funding for its laboratory testing programs at selected universities, medical schools and hospitals for the purpose of developing additional uses of Hextend, PentaLyte, HetaCool, and other new products, but the amount of research that will be conducted at those institutions will depend upon the Company's financial status.

The Company was incorporated under the laws of the State of California on November 30, 1990. The Company's principal office is located at 935 Pardee Street, Berkeley, California 94710. Its telephone number at such office is (510) 845-9535.

Hextend® and PentaLyte® are registered trademarks, and HetaCool™ is a trademark, of BioTime, Inc.

## **Products for Surgery, Plasma Volume Replacement and Emergency Care**

### *The Market for Plasma Volume Expanders*

The Company is developing Hextend, PentaLyte, HetaCool and other synthetic plasma expander solutions to treat acute blood loss that occurs as a result of trauma injuries and during many kinds of surgery. These products are synthetic, can be sterilized, and can be manufactured in large volumes. Hextend, PentaLyte, and HetaCool contain constituents that may maintain physiological balance when used to replace lost blood volume.

Hextend is also currently being used to treat hypovolemia subsequent to trauma or sepsis by emergency room physicians. After appropriate clinical testing and regulatory approval, it may be used by paramedics to treat acute blood loss in trauma victims being transported to the hospital. Hextend has also been purchased by the United States armed forces and may be used in cases of battlefield trauma.

Approximately 10,000,000 surgeries take place in the United States each year, and blood transfusions are required in approximately 3,000,000 of those cases. Transfusions are also required to treat patients suffering severe blood loss due to traumatic injury. Many more surgical and trauma cases do not require blood transfusions but do involve significant bleeding that can place the patient at risk of suffering from shock caused by the loss of fluid volume (hypovolemia) and physiological balance. Whole blood and packed red cells generally cannot be administered to a patient until the patient's blood has been typed and sufficient units of compatible blood or red cells can be located. Periodic shortages of supply of donated human blood are not uncommon, and rare blood types are often difficult to locate. The use of human blood products also poses the risk of exposing the patient to blood borne diseases such as AIDS and hepatitis.

Due to the risks and cost of using human blood products, even when a sufficient supply of compatible blood is available, physicians treating patients suffering blood loss are generally not permitted to transfuse red blood cells until the patient's level of red blood cells has fallen to a level known as the transfusion trigger. During the course of surgery, while blood volume is being lost, the patient is infused with plasma volume expanders to maintain adequate blood circulation. During the surgical procedure, red blood cells are not generally replaced until the patient has lost approximately 45% to 50% of their red blood cells, thus reaching the transfusion trigger at which point the transfusion of red blood cells may be required. After the transfusion of red blood cells, the patient may continue to experience blood volume loss, which will be replaced with plasma volume expanders. Even in those patients who do not require a transfusion, physicians routinely administer plasma volume expanders to maintain sufficient fluid volume to permit the available red blood cells to circulate throughout the body and to maintain the patient's physiological balance.

Several units of fluid replacement products are often administered during surgery. The number of units will vary depending upon the amount of blood loss and the kind of plasma volume expander administered. Crystalloid products must be used in larger volumes than colloid products such as Hextend.

*The Market for Products for Hypothermic Surgery*

In 1997, more than 500,000 coronary bypass and other open heart surgeries were performed in the United States annually. Approximately 18,000 aneurysm surgeries and 4,000 arterio-venous malformation surgeries were performed in the United States during 1989. Current estimates indicate that more than one million people over age 55 have pathological changes associated with aortic arch aneurysms. Open heart procedures often require the use of cardio-pulmonary bypass equipment to do the work of the heart and lungs during the surgery. During open heart surgery and surgical procedures for the treatment of certain cardiovascular conditions such as large aneurysms, cardiovascular abnormalities and damaged blood vessels in the brain, surgeons must temporarily interrupt the flow of blood through the body. Interruption of blood flow can be maintained only for short periods of time at normal body temperatures because many critical organs, particularly the brain, are quickly damaged by the resultant loss of oxygen. As a result, certain surgical procedures are performed at low temperatures because lower body temperature helps to minimize the chance of damage to the patient's organs by reducing the patient's metabolic rate, thereby decreasing the patient's needs during surgery for oxygen and nutrients which normally flow through the blood.

Current technology limits the degree to which surgeons can lower a patient's temperature and the amount of time the patient can be maintained at a low body temperature because blood, even when diluted, cannot be circulated through the body at near-freezing temperatures. As a result, surgeons face severe time constraints in performing surgical procedures requiring blood flow interruption, and those time limitations prevent surgeons from correcting certain cardiovascular abnormalities.

Hypothermic techniques may also have an important use in treating trauma patients that have experienced severe blood loss. BioTime is sponsoring a new project at the State University of New York Health Sciences Center in Brooklyn to study hypothermia and complete blood volume replacement with HetaCool in an animal model of civilian trauma.

*Hextend, PentaLyte and HetaCool*

The Company's first three blood volume replacement products, Hextend, PentaLyte, and HetaCool have been formulated to maintain the patient's tissue and organ function by sustaining the patient's fluid volume and physiological balance. Hextend, PentaLyte, and HetaCool, are composed of a hydroxyethyl starch, electrolytes, sugar and lactate in an aqueous base. Hextend and HetaCool use a high molecular weight hydroxyethyl starch (hetastarch) whereas PentaLyte uses a lower, molecular weight hydroxyethyl starch (pentastarch). The hetastarch is retained in the blood longer than the pentastarch, which may make Hextend and HetaCool the products of choice when a larger volume of plasma expander or blood replacement solution for low temperature surgery is needed or where the patient's ability to restore his own blood proteins after surgery is compromised. PentaLyte, with pentastarch, would be eliminated from the blood faster than Hextend and HetaCool and might be used when less plasma expander is needed or where the patient is more capable of quickly restoring lost blood proteins. The Company has also tested HexaLyte, a new plasma volume expander that contains a low molecular weight hydroxyethyl starch and that would be eliminated



from the body more rapidly than Hextend and HetaCool, but not as rapidly as PentaLyte. BioTime believes that by testing and bringing these products to the market, it can increase its market share by providing the medical community with solutions to match patients' needs.

Certain clinical test results indicate that Hextend is effective at maintaining blood calcium levels when used to replace lost blood volume. Calcium can be a significant factor in regulating blood clotting and cardiac function. Clinical studies have also shown that Hextend maintains acid-base better than saline-based surgical fluids. The Company expects that PentaLyte will also be able to maintain blood calcium levels and acid-base balance based upon laboratory studies and the fact that the formulation of PentaLyte is similar to that of Hextend.

On June 14, 2002, the Blood Products Advisory Committee of the United States Food and Drug Administration voted 8-0 with 2 abstentions to recommend to the FDA that the labeling of 6% hetastarch in saline should be changed by adding a warning regarding the risk of bleeding during cardiac surgery. 6% hetastarch in saline solution is a plasma volume expander that competes in the market with Hextend. No such recommendation was made for Hextend since it is a different product.

Albumin produced from human plasma is also used as plasma volume expander, but it is expensive and subject to supply shortages. Additionally, an FDA warning has cautioned physicians about the risk of administering albumin to seriously ill patients.

BioTime has not attempted to synthesize potentially toxic and costly oxygen carrying molecules such as hemoglobin because the loss of fluid volume and physiological balance may contribute as much to shock as the loss of the oxygen carrying component of the blood. Surgical and trauma patients are routinely given supplemental oxygen and retain a substantial portion of their own red blood cells. Whole blood or packed red blood cells are generally not transfused during surgery or in trauma care until several units of plasma volume expanders have been administered and the patient's hematocrit has fallen to the transfusion trigger. Therefore, the lack of oxygen carrying molecules in the Company's solutions should not pose a significant contraindication to use.

However, BioTime scientists have conducted laboratory animal experiments in which they have shown that Hextend can be successfully used in conjunction with a hemoglobin-based oxygen carrier solution approved for veterinary purposes to completely replace the animal's circulating blood volume without any subsequent transfusion and without the use of supplemental oxygen. By diluting these oxygen carrier solutions, Hextend may reduce the potential toxicity and costs associated with the use of those products. Once such solutions have received regulatory approval and become commercially available, this sort of protocol may prove valuable in markets in parts of the developing world where the blood supply is extremely unsafe. These applications may also be useful in combat where logistics make blood use impracticable.

**Hextend** is BioTime's proprietary hetastarch-based synthetic blood plasma volume expander, designed especially to treat hypovolemia in surgery where patients experience significant blood loss. An important goal of the Hextend development program was to produce a product that can be used in multi-liter volumes. The safety related secondary endpoints targeted in the U.S. clinical study included those involving coagulation. The Company believes that the low incidence of adverse

events related to blood clotting in the Hextend patients demonstrates that Hextend may be safely used in amounts exceeding 1.5 liters. An average of 1.6 liters of Hextend was used in the Phase III clinical trials, with an average of two liters for patients who received transfused blood products. Since then, more than half a million units (500 mL bags) have been sold for commercial purposes, and the use of quantities of 7 to 8 liters per patient have been reported. There have been no serious adverse events directly related to the use of Hextend even when used in these large volumes.

Hextend is also being used in surgery with cardio-pulmonary bypass circuits. In order to perform heart surgery, the patient's heart must be stopped and a mechanical apparatus is used to oxygenate and circulate the blood. The cardio-pulmonary bypass apparatus requires a blood compatible fluid such as Hextend to commence and maintain the process of diverting the patient's blood from the heart and lungs to the mechanical oxygenator and pump. In a recent clinical trial, cardiac surgery patients treated with Hextend, maintained more normal kidney function, experienced less pain and nausea, showed no deep venous thromboses, avoided dialysis, and had shorter delay times to first meal compared to those treated with other fluids.

**PentaLyte** is BioTime's proprietary pentastarch-based synthetic plasma expander, designed especially for use when a faster elimination of the starch component is desired and acceptable. Although Hextend can be used in these cases, some physicians appear to prefer a solution which could be metabolized faster and excreted earlier when the longer term protection provided by Hextend is not required. PentaLyte combines the physiologically balanced Hextend formulation with pentastarch that has a lower molecular weight and degree of substitution than the hetastarch used in Hextend. Plasma expanders containing pentastarch are currently widely used around the world. BioTime has completed its Phase I clinical study and is planning more advanced PentaLyte clinical trials. BioTime's present plan is to seek approval of PentaLyte for use in the treatment of hypovolemia.

**HetaCool** is a modified formulation of Hextend. HetaCool is specifically designed for use at low temperatures. Surgeons are already using Hextend and a variety of other solutions to carry out certain limited procedures involving shorter term (up to nearly one hour) arrest of brain and heart function at temperatures between 15° and 25° C. However, BioTime is not aware of any fluid currently used in medical practice or any medically-approved protocol allowing operations which can completely replace all of a patient's blood at temperatures close to the ice point. The Company believes that very low temperature bloodless surgical techniques could be developed for open heart and minimally invasive closed chest cardiovascular surgeries, removal of tumors from and the repair of aneurysms in the brain, heart, and other areas, as well as in the treatment of trauma, toxicity and cancer.

The Company is in the process of preparing an amendment to its Hextend IND application to conduct clinical trials using HetaCool as a solution to replace all of a patient's circulating blood volume during profound hypothermic (carried out at near-freezing temperatures) surgical procedures. The experimental protocol for the planned blood replacement clinical trial is being tested on animal

subjects. HetaCool would be introduced into the patient's body during the cooling process. Once the patient's body temperature is nearly ice cold, and heart and brain function are temporarily arrested, the surgeon would perform the operation. During the surgery, HetaCool may be circulated throughout the body in place of blood, or the circulation may be arrested for a period of time if an interruption of fluid circulation is required. Upon completion of the surgery, the patient would be slowly warmed and blood would be transfused.

Cardiac surgeons are working to develop innovative procedures to repair damaged coronary arteries and heart valves. If optically guided surgical instruments can be inserted into the heart through blood vessels or small incisions, there may be no need to open the patient's chest cavity. BioTime believes that HetaCool may be useful in these minimally invasive closed chest cardiac procedures because the solution is transparent and if it were used to completely replace blood at low temperatures it would permit surgeons to use their optically guided instruments inside the heart or blood vessels without having their view obstructed by blood. The use of BioTime's solutions may also allow better control over stopping and starting the heart, as well as extending the time period of such surgeries.

HetaCool has been used to completely replace the blood volume of hamsters, dogs, pigs, and baboons at temperatures approaching freezing. Many of these animal subjects survived long term after hypothermic blood substitution with HetaCool. In these laboratory tests, the animals' blood was replaced by HetaCool and they were chilled for one to more than four hours with deep body temperatures between 1°C and 10°C. Hextend was used to partially replace blood during cancer surgery in which a patient's body temperature was lowered to 1°C and his heart was stopped for 27 minutes while the tumor was removed. The patient recovered without incident, and a case study of the procedure was published in the April 2002 of the Canadian Journal of Anesthesia.

BioTime has recently launched a research program using HetaCool in animal models of trauma at the State University of New York Health Science Center in Brooklyn. Preliminary laboratory results there have already supported the feasibility of using HetaCool to treat subjects following severe hemorrhage. The use of HetaCool at near-freezing temperatures also will be studied in animal models of cardiovascular surgery at the Texas Heart Institute in Houston. The project has been approved by the appropriate internal committees, and is awaiting the beginning of experimentation.

BioTime is developing a new formulation that has allowed the revival of hamsters after as long as 6.5 hours of hypothermic blood substitution during which time the animals' heartbeat and circulation were stopped.

## Organ Transplant Products

### *The Market for Organ Preservation Solutions*

Organ transplant surgery is a growing field. Each year in the United States, approximately 5,000 donors donate organs, and approximately 5,000 people donate skin, bone and other tissues. As more surgeons have gained the necessary expertise and surgical methods have been refined, the number of transplant procedures has increased, as has the percentage of successful transplants. Organ transplant surgeons and their patients face two major obstacles, namely the shortage of available organs from donors, and the limited amount of time that a transplantable organ can be kept viable between the time it is harvested from the donor and the time it is transplanted into the recipient.

The scarcity of transplantable organs makes them too precious to lose and increases the importance of effective preservation technology and products. Current organ removal and preservation technology generally requires multiple preservation solutions to remove and preserve effectively different groups of organs. The removal of one organ can impair the viability of other organs. Available technology does not permit surgeons to keep the remaining organs viable within the donor's body for a significant time after the first organ is removed. Currently, an organ available for transplant is flushed with an ice cold solution during the removal process to deactivate the organ and preserve its tissues, and then the organ is transported on ice to the donee. The ice cold solutions currently used, together with transportation on ice, keep the organ healthy for only a short period of time. For example, the storage time for hearts is limited to approximately six hours. Because of the short time span available for removal and transplant of an organ, potential organ donees may not receive the needed organs.

BioTime is seeking to address this problem by developing a more effective organ preservation solution that will permit surgeons to harvest all transplantable organs from a single donor. The Company believes that preserving the viability of all transplantable organs and tissues simultaneously, at low temperatures, would extend by several hours the time span in which the organs can be preserved prior to transplant.

**Using HetaCool for Multi-Organ Preservation.** The Company is seeking to develop HetaCool for use as a single solution that can simultaneously preserve all of a single donor's organs. When used as an organ preservation solution, HetaCool would be perfused into the donor's body while the body is chilled, thereby eliminating an undesirable condition called warm ischemia, caused when an organ is warm while its blood supply is interrupted. The use of HetaCool in conjunction with the chilling of the body should help to slow down the process of organ deterioration by a number of hours so that a surgeon can remove all organs for donation and transplant. The Company's current estimates are that each such preservation procedure could require as much as 50 liters of HetaCool.

The Company believes that the ability to replace an animal's blood with the Company's HetaCool solution, to maintain the animal at near freezing temperatures for several hours, and then revive the animal, would demonstrate that the solution could be used for multi-organ preservation.

Company scientists have revived animals after more than six hours of cold blood-substitution, and have observed heart function in animals maintained cold and blood-substituted for more than eight hours. An objective of the Company's research and development program is to extend the time span in which animal subjects can be maintained in a cold, blood-substituted state before revival or removal of organs for transplant purposes. Organ transplant procedures using animal subjects could then be conducted to test the effectiveness of Hextend as an organ preservative.

A successful transplant of a lung cooled inside the donor's body prior to transplant has recently been reported in Sweden. The patient who received the lung was reported to be doing well several months later. The success of that transplant, which did not involve the use of a BioTime product, involved the preservation and transplant of a single organ, but indicates that hypothermic techniques can be used to preserve organs in the donor prior to removal for transplant.

#### *Long-term Tissue and Organ Banking*

The development of marketable products and technologies for the preservation of tissues and vital organs for weeks and months is a long-range goal of the Company's research and development plan. To permit such long-term organ banking the Company is attempting to develop products and technologies that can protect tissues and organs from the damage that occurs when human tissues are subjected to subfreezing temperatures.

**HetaFreeze** is one of a family of BioTime's freeze-protective solutions which may ultimately allow the extension of time during which organs and tissues can be stored for future transplant or surgical grafting. In laboratory experiments, BioTime's proprietary freeze-protective compounds have already been used to preserve skin when used as a whole animal perfusate. Silver dollar size full thickness shaved skin samples have been removed after saturation with HetaFreeze solution, frozen at liquid nitrogen temperatures and stored for periods ranging from days to weeks. The grafts were then warmed and sewn onto the backs of host animals. Many of these grafts survived. In more recent experiments, rat femoral arteries were frozen to liquid nitrogen temperatures, later thawed and then transplanted into host rats. These grafts were proven to last up to four months. The work was published in the October 2002 issue of the *Annals of Plastic Surgery*.

In other laboratory experiments, BioTime scientists have shown that animals can be revived to consciousness after partial freezing with their blood replaced by HetaFreeze. While this technology has not developed to an extent that allows long term survival of the laboratory subjects, and their organs, a better understanding of the effects of partial freezing could allow for extended preservation times for vital organs, skin and blood vessels.

#### **Other Potential Uses of BioTime Solutions**

Isolated regional perfusion of anti-cancer drugs has been used to treat melanoma of the limbs, and inoperable tumors of the liver. The Company believes that employing such a procedure while the patient is kept in ice-cold blood-substitution may allow high doses of toxic anti-cancer drugs to be directed at inoperable tumors within vital organs, which would selectively be warmed. Keeping the rest of the patient in a cold, blood substituted state may reduce or eliminate the circulation of the toxic drugs to healthy tissues.

BioTime considers such surgical techniques to be a longer range goal of its research and development program for hypothermic surgery products. Use of this complex technology in the practice of oncology can occur only after ice-cold blood-substitution has advanced to an appropriate level of safety and effectiveness.

### **Research and Development Strategy**

From inception through December 31, 2002, the Company has expensed \$22,734,008 on research and development. The greatest portion of BioTime's research and development efforts have been devoted to the development of Hextend, PentaLyte and HetaCool for conventional surgery, emergency care, low temperature surgery, and multi-organ preservation. A lesser portion of the Company's research and development efforts have been devoted to developing solutions and protocols for storing organs and tissues at subfreezing temperatures. In the future the Company may explore other applications of its products and technologies, including cancer chemotherapy. As the first products achieve market entry, more effort will be expended to bring the next tier of products to maturity.

A major focus of the Company's research and development effort has been on products and technology to significantly reduce or eliminate the need for blood products in surgery and trauma care. The Company has recently conducted preliminary studies using Hextend in a pressurized oxygen environment and found that Hextend can replace nearly all, or in some cases all, of the circulating blood of rats. Some of the rats were able to live long term without a subsequent transfusion, while others received their own blood back. In other cases, Hextend was used in large volumes in association with a hemoglobin-based oxygen carrier solution approved for veterinary use. When used in this way, rats were able to live long term after all their circulating blood was replaced at normal body temperature breathing room air.

In still other experiments, rats were allowed to lose approximately half their circulating blood volume, and then allowed to develop and remain in respiratory arrest from 10-18 minutes. They were then resuscitated with Hextend and either ventilated with 100% oxygen, or in a hyperbaric oxygen chamber containing 100% oxygen at two atmospheres above normal pressure. Some of the rats recovered and lived long term after as long as 15 minutes of respiratory arrest. The hyperbaric chamber appeared to have improved the outcome in a number of cases.

These studies indicate that Hextend can potentially be used in a variety of protocols in which donor blood is difficult or impossible to use, such as on the battlefield, or in parts of the world where there is a shortage of disease-free blood.

Another major focus of the Company's research and development effort has been on products and technology to extend the time animals can be kept cold and blood-substituted, and then revived without physical impairment. An integral part of that effort has been the development of techniques and procedures or protocols for use of the Company's products. A substantial amount of data has been accumulated through animal tests, including the proper surgical techniques, drugs and anesthetics, the temperatures and pressures at which blood and blood replacement solutions should be removed, restored and circulated, solution volume, the temperature range, and times, for maintaining circulatory arrest, and the rate at which the subject should be rewarmed.

Experiments intended to test the efficacy of the Company's low temperature blood replacement solutions and protocols for surgical applications involve replacing the animal's blood with the Company's solution, maintaining the animal in a cold blood-substituted state for a period of time, and then attempting to revive the animal. Experiments for multi-organ preservation involve the maintenance of the animal subjects at cold temperatures for longer periods of time than would be required for many surgical applications, followed by transplant procedures to test the viability of one or more of the subject's vital organs.

The Company is conducting experiments at hospitals, medical schools, and university research facilities. These collaborative research programs are testing solutions and protocols developed in the Company's laboratories and, in some cases, comparing the efficacy of the Company's products with commercially available FDA approved products manufactured by other companies. Collaborative gerontological research is being conducted at the University of California at Berkeley. The Company intends to continue to foster relations with research hospitals and medical schools for the purpose of conducting collaborative research projects because it believes that such projects will introduce the Company's potential products to members of the medical profession and provide the Company with objective product evaluations from independent research physicians and surgeons.

BioTime has also expanded its product development efforts by initiating an interventive gerontology program focused on the identification of specific factors central to aging of the brain. The program, which is being undertaken with the cooperation of the University of California at Berkeley, is focused on the development of medical and pharmacological strategies to treat senescence related consequences.

#### **Licensing**

##### *Abbott Laboratories*

On April 23, 1997, the Company and Abbott entered into a License Agreement under which the Company granted to Abbott an exclusive license to manufacture and sell Hextend in the United States and Canada for all therapeutic uses other than those involving hypothermic surgery where the patient's body temperature is lower than 12°C ( Hypothermic Use ), or replacement of substantially all of a patient's circulating blood volume ( Total Body Washout ). The Company has retained all rights to manufacture, sell or license Hextend and other products in all other countries.

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Under the Abbott License Agreement, Abbott has agreed to pay the Company up to \$40,000,000 in license fees, of which \$2,500,000 has been paid to date for the grant of the license and the achievement of certain milestones. Up to \$37,500,000 of additional license fees will be payable based upon annual net sales of Hextend, at the rate of 10% of annual net sales if annual net sales exceed \$30,000,000 or 5% if annual net sales are between \$15,000,000 and \$30,000,000. Abbott's obligation to pay licensing fees on sales of Hextend will expire on the earlier of January 1, 2007 or, on a country by country basis, when all patents protecting Hextend in the applicable country expire or any third party obtains certain regulatory approvals to market a generic equivalent product in that country.

In addition to the license fees, Abbott will pay the Company a royalty on total annual net sales of Hextend. The royalty rate will be 5% plus an additional .22% for each \$1,000,000 of annual net sales, up to a maximum royalty rate of 36%. The royalty rate for each year will be applied on a total net sales basis. Abbott's obligation to pay royalties on sales of Hextend will expire in the United States or Canada when all patents protecting Hextend in the applicable country expire and any third party obtains certain regulatory approvals to market a generic equivalent product in that country.

Abbott has agreed that the Company may convert Abbott's exclusive license to a non-exclusive license or may terminate the license outright if certain minimum sales and royalty payments are not met. In order to terminate the license outright, the Company would pay a termination fee in an amount ranging from the milestone payments made by Abbott to an amount equal to three times prior year net sales, depending upon when termination occurs. Abbott's exclusive license also may terminate, without the payment of termination fees by the Company, if Abbott fails to market Hextend. Abbott has agreed to manufacture Hextend for sale by the Company in the event that Abbott's exclusive license is terminated in either case.

Abbott has certain rights to acquire additional licenses to manufacture and sell the Company's other plasma expander products in the United States and Canada. If Abbott exercises these rights to acquire a license to sell such products for uses other than Hypothermic Surgery or Total Body Washout, in addition to paying royalties, Abbott will be obligated to pay a license fee based upon the Company's direct and indirect research, development and other costs allocable to the new product. If Abbott desires to acquire a license to sell any of the Company's products for use in Hypothermic Surgery or Total Body Washout, the license fees and other terms of the license will be subject to negotiation between the parties. For the purpose of determining the applicable royalty rates, net sales of any such new products licensed by Abbott will be aggregated with sales of Hextend. If Abbott does not exercise its right to acquire a new product license, the Company may manufacture and sell the product itself or may license others to do so.

In order to preserve its rights to obtain an exclusive license for PentaLyte under its License Agreement, Abbott notified the Company that Abbott will supply BioTime with batches of PentaLyte, characterization and stability studies, and other regulatory support needed for BioTime to file an IND and conduct clinical studies.

The foregoing description of the Abbott License Agreement is a summary only and is qualified in all respects by reference to the full text of that License Agreement.

### *CJ Corp.*

On March 27, 2003, the Company and CJ entered into the CJ Agreement under which the Company granted to CJ an exclusive license to manufacture and sell Hextend and PentaLyte in the Republic of Korea for human therapeutic uses at temperatures above 12°C.

Under the CJ Agreement, the Company will receive a license fee of \$800,000, to be paid in two installments, including a payment of \$500,000 within 30 days after the signing of the CJ Agreement and \$300,000 within 30 days after an application for regulatory approval to manufacture and market Hextend is filed in Korea. CJ will be responsible for obtaining the regulatory approvals required to manufacture and market Hextend and PentaLyte, including conducting any clinical trials that may be required, and will bear all related costs and expenses.

In addition to the license fees, CJ will pay the Company a royalty on sales of the licensed products. The royalty will range from \$1.30 to \$2.60 per 500 mL unit of product sold, depending upon the price approved by Korea's National Health Insurance. Royalties will be paid quarterly. CJ's obligation to pay royalties on sales of Hextend will expire when all patents protecting Hextend in Korea expire or any third party obtains regulatory approvals to market a generic equivalent product in Korea, whichever first occurs.

The Company may convert CJ's exclusive license to a non-exclusive license if certain minimum sales and royalty payments are not met.

CJ has right of first refusal to acquire additional licenses to manufacture and sell the Company's other plasma expander products in Korea.

The foregoing description of the CJ Agreement is a summary only and is qualified in all respects by reference to the full text of the CJ Agreement.





*Other Licensing Efforts*

The Company is discussing prospective licensing arrangements with other pharmaceutical companies that have expressed their interest in marketing the Company's products abroad. In licensing arrangements that include marketing rights, the participating pharmaceutical company would be entitled to retain a large portion of the revenues from sales to end users and would pay the Company a royalty on net sales. There is no assurance that any such licensing arrangements can be made.

**Manufacturing**

*Manufacturing Arrangements*

Abbott manufactures Hextend for the North American market, and NPBI International, BV, a Netherlands company ( NPBI ), has manufactured lots of Hextend for the Company's use in seeking regulatory approval in Europe. Abbott and NPBI have the facilities to manufacture Hextend and other BioTime products in commercial quantities. If Abbott chooses not to obtain a license to manufacture and market another BioTime product, and if NPBI declines to manufacture BioTime products on a commercial basis, other manufacturers will have to be found that would be willing to manufacture products for BioTime or any licensee of BioTime products.

*Facilities Required*

Any products that are used in clinical trials for regulatory approval in the United States or abroad, or that are approved by the FDA or foreign regulatory authorities for marketing, have to be manufactured according to good manufacturing practices at a facility that has passed regulatory inspection. In addition, products that are approved for sale will have to be manufactured in commercial quantities, and with sufficient stability to withstand the distribution process, and in compliance with such domestic and foreign regulatory requirements as may be applicable. The active ingredients and component parts of the products must be either USP or themselves manufactured according to good manufacturing practices.

The Company does not have facilities to manufacture its products in commercial quantities, or under good manufacturing practices. Acquiring a manufacturing facility would involve significant expenditure of time and money for design and construction of the facility, purchasing equipment, hiring and training a production staff, purchasing raw material and attaining an efficient level of production. Although the Company has not determined the cost of constructing production facilities that meet FDA requirements, it expects that the cost would be substantial, and that the Company would need to raise additional capital in the future for that purpose. To avoid the incurrence of those expenses and delays, the Company is relying on contract and licensing arrangements with established pharmaceutical companies for the production of the Company's products, but there can be no assurance that satisfactory arrangements will be made for any new products that the Company may develop.

### *Raw Materials*

Although most ingredients in the products being developed by the Company are readily obtainable from multiple sources, the Company knows of only a few manufacturers of the hydroxyethyl starches that serve as the drug substance in Hextend, PentaLyte and HetaCool. Abbott presently has a source of supply of the hydroxyethyl starch used in Hextend, PentaLyte and HetaCool, and has agreed to maintain a supply sufficient to meet market demand for Hextend in the United States and Canada. The Company believes that it will be able to obtain a sufficient supply of starch for its needs in the foreseeable future, although the Company does not have supply agreements in place. If for any reason a sufficient supply of hydroxyethyl starch could not be obtained, the Company or a licensee would have to acquire a manufacturing facility and the technology to produce the hydroxyethyl starch according to good manufacturing practices. The Company would have to raise additional capital to participate in the development and acquisition of the necessary production technology and facilities.

If arrangements cannot be made for a source of supply of hydroxyethyl starch, the Company would have to reformulate its solutions to use one or more other starches that are more readily available. In order to reformulate its products, the Company would have to perform new laboratory testing to determine whether the alternative starches could be used in a safe and effective synthetic plasma volume expander, low temperature blood substitute or organ preservation solution. If needed, such testing would be costly to conduct and would delay the Company's product development program, and there is no certainty that any such testing would demonstrate that an alternative ingredient, even if chemically similar to the one currently used, would be as safe or effective.

### **Marketing**

Hextend is being sold by Abbott in the United States. Regulatory approval has been obtained in Canada, where Abbott is on the verge of launching the product.

Hextend has been approved for use and added to hospital formularies in hundreds of hospitals. Inclusion on hospital formularies is important because it enables physicians to obtain Hextend without the need to special order it.

BioTime recently granted CJ the right to manufacture and market Hextend and PentaLyte in Korea, but CJ will have to obtain regulatory approvals before it can market either product.

Because Hextend is a surgical product, sales efforts must be directed to physicians and hospitals. The Hextend marketing strategy is designed to reach its target customer base through sales calls and an advertising campaign focused on the use of a plasma-like substance to replace lost blood volume and the ability of Hextend to support vital physiological processes.

Hextend competes with other products used to treat or prevent hypovolemia, including albumin, generic 6% hetastarch solutions, and crystalloid solutions. The competing products have been commonly used in surgery and trauma care for many years, and in order to sell Hextend, physicians must be convinced to change their product loyalties. Although albumin is expensive, crystalloid solutions and generic 6% hetastarch solutions sell at low prices. In order to compete with other products, particularly those that sell at lower prices, Hextend will have to be recognized as providing medically significant advantages.

The Blood Products Advisory Committee of the FDA has recommended to the FDA that the labeling of 6% hetastarch in saline should be changed by adding a warning regarding the risk of bleeding during cardiac surgery. No such recommendation was made for Hextend since it is a different product. An article discussing the meeting entitled "6% Hetastarch in Saline Linked To Excessive Bleeding in Bypass Surgery" appeared in the December 2002 edition of *Anesthesiology News*. BioTime understands that a number of hospitals have switched from 6% hetastarch in saline to Hextend due to these concerns.

As part of the marketing program, a number of studies have been conducted that show the advantages of receiving Hextend and other BioTime products during surgery. As these studies are completed, the results are presented at medical conferences and articles written for publication in medical journals. The Company is also aware of independent studies using Hextend that are being conducted by physicians and hospitals who may publish their findings in medical journals or report their findings at medical conferences. The outcome of future medical studies and timing of the publication or presentation of the results could have an effect on Hextend sales.

### **Government Regulation**

The FDA and foreign regulatory authorities will regulate the Company's proposed products as drugs, biologicals, or medical devices, depending upon such factors as the use to which the product will be put, the chemical composition and the interaction of the product on the human body. In the United States, products that are intended to be introduced into the body, such as blood substitute solutions for low temperature surgery and plasma expanders, will be regulated as drugs and will be reviewed by the FDA staff responsible for evaluating biologicals.

The Company's domestic human drug products will be subject to rigorous FDA review and approval procedures. After testing in animals, an IND application must be filed with the FDA to obtain authorization for human testing. Extensive clinical testing, which is generally done in three phases, must then be undertaken at a hospital or medical center to demonstrate optimal use, safety and efficacy of each product in humans. Each clinical study is conducted under the auspices of an independent Institutional Review Board (IRB). The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. The time and expense required to perform this clinical testing can far exceed the time and expense of the research and development initially required to create the product. No action can be taken to market any therapeutic product in the United States until an appropriate New Drug Application (NDA) has been approved by the FDA. Even after initial FDA approval has been obtained, further studies may be required to provide additional data on safety or to gain approval for the use of a product as a treatment for clinical indications other than those initially targeted. In addition, use of these products during testing and after marketing could reveal side effects that could delay, impede or prevent FDA marketing approval, resulting in a FDA-ordered product recall, or in FDA-imposed limitations on permissible uses.

The FDA regulates the manufacturing process of pharmaceutical products, requiring that they be produced in compliance with good manufacturing practices. See *Manufacturing*. The FDA also regulates the content of advertisements used to market pharmaceutical products. Generally,

claims made in advertisements concerning the safety and efficacy of a product, or any advantages of a product over another product, must be supported by clinical data filed as part of an NDA or an amendment to an NDA, and statements regarding the use of a product must be consistent with the FDA approved labeling and dosage information for that product.

Sales of pharmaceutical products outside the United States are subject to foreign regulatory requirements that vary widely from country to country. Even if FDA approval has been obtained, approval of a product by comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing the product in those countries. The time required to obtain such approval may be longer or shorter than that required for FDA approval.

#### **Patents and Trade Secrets**

The Company currently holds 21 issued United States patents having composition and methods of use claims covering BioTime's proprietary solutions, including Hextend and PentaLyte. The most recent U.S. patents were issued during 2002. Some of BioTime's allowed claims in the United States, which include the composition and methods of use of Hextend and PentaLyte, are expected to remain in force until 2019. Forty patents covering certain of the Company's solutions have also been issued in the countries of the European Union, Australia, Israel, Russia, Hong Kong, South Africa, Japan, and South Korea. Additional patent applications have been filed in the United States and numerous other countries for Hextend, PentaLyte and other solutions. Certain device patents describing BioTime's hyperbaric chamber, and proprietary microcannula have also been issued in the United States and overseas, both of which although only used in research so far have possible indications in clinical medicine.

There is no assurance that any additional patents will be issued, or that any patents now held or later obtained by the Company will not be successfully challenged by third parties and declared invalid or infringing of third party claims. Further, the enforcement of patent rights often requires litigation against third party infringers, and such litigation can be costly to pursue.

In addition to patents, the Company will rely on trade secrets, know-how and continuing technological advancement to maintain its competitive position. The Company has entered into intellectual property, invention and non-disclosure agreements with its employees and it is the Company's practice to enter into confidentiality agreements with its consultants. There can be no assurance, however, that these measures will prevent the unauthorized disclosure or use of the Company's trade secrets and know-how or that others may not independently develop similar trade secrets and know-how or obtain access to the Company's trade secrets, know-how or proprietary technology.

#### **Competition**

The Company's solutions will compete with products currently used to treat or prevent hypovolemia, including albumin, other colloid solutions, and crystalloid solutions presently manufactured by established pharmaceutical companies, and with human blood products. Some of these products, in particular crystalloid solutions, are commonly used in surgery and trauma care and sell at low prices. In order to compete with other products, particularly those that sell at lower prices, the Company's products will have to be recognized as providing medically significant advantages. Like Hextend, the competing products are being manufactured and marketed by established pharmaceutical companies that have large research facilities, technical staffs and financial and marketing resources. B.Braun presently markets Hespan, an artificial plasma volume expander containing 6% hetastarch in saline solution. Abbott and Baxter International manufacture and sell a generic equivalent of Hespan. As a result of the introduction of generic plasma expanders intended to compete with Hespan, competition in the plasma expander market has intensified and wholesale prices have declined. Abbott, which markets Hextend for BioTime in the United States, is also the leading seller of generic 6% hetastarch in saline solution. Aventis Behring, LLC, Baxter International, and Alpha Therapeutics sell albumin, and Abbott, Baxter International and B.Braun sell crystalloid solutions

To compete with new and existing plasma expanders, the Company has developed products that contain constituents that may prevent or reduce the physiological imbalances, bleeding, fluid overload, edema, poor oxygenation, and organ failure that can occur when competing products are used. To compete with existing organ preservation solutions, the Company has developed solutions that can be used to preserve all organs simultaneously and for long periods of time.

A number of other companies are known to be developing hemoglobin and synthetic red blood cell substitutes and technologies. BioTime's products have been developed for use either before red blood cells are needed or in conjunction with the use of red blood cells. In contrast, hemoglobin and other red blood cell substitute products are designed to remedy ischemia and similar conditions that may result from the loss of oxygen carrying red blood cells. Those products would not necessarily compete with the Company's products unless the oxygenating molecules were included in solutions that could replace fluid volume and prevent or reduce the physiological imbalances as effectively as the Company's products. Generally, red blood cell substitutes are more expensive to produce and potentially more toxic than Hextend and PentaLyte.

Competition in the areas of business targeted by the Company is likely to intensify further as new products and technologies reach the market. Superior new products are likely to sell for higher prices and generate higher profit margins once acceptance by the medical community is achieved. Those companies that are successful in introducing new products and technologies to the market first may gain significant economic advantages over their competitors in the establishment of a customer base and track record for the performance of their products and technologies. Such companies will also benefit from revenues from sales which could be used to strengthen their research and development, production, and marketing resources. All companies engaged in the medical products industry face the risk of obsolescence of their products and technologies as more advanced or cost effective products and technologies are developed by their competitors. As the industry matures, companies will compete based upon the performance and cost effectiveness of their products.

## Employees

As of December 31, 2002, the Company employed seven persons on a full-time basis and two persons on a part-time basis. Three full-time employees and one part-time employee hold Ph.D. Degrees in one or more fields of science.

## Risk Factors

Some of the factors that could materially affect the Company's operations and prospects are discussed below. There may be other factors that are not mentioned here or of which BioTime is not presently aware that could also affect BioTime's operations.

### *BioTime May Not Succeed In Marketing Its Products Due to the Availability of Competing Products*

BioTime's ability to generate operating revenue depends upon its success in developing and marketing its products. BioTime may not succeed in marketing its products and may not receive sufficient revenues from product sales to meet operating expenses or to earn a profit. In this regard, sales of Hextend to date have not been sufficient to generate an amount of royalties or licensing fees sufficient to cover BioTime's operating expenses. Factors that affect the marketing of the Company's products include the following:

Hextend and BioTime's other plasma expander products will compete with other products that are commonly used in surgery and trauma care and sell at low prices.

In order to compete with other products, particularly those that sell at lower prices, BioTime products will have to provide medically significant advantages.

Physicians and hospitals may be reluctant to try a new product due to the high degree of risk associated with the application of new technologies and products in the field of human medicine.

Competing products are being manufactured and marketed by established pharmaceutical companies. For example, B. Braun/McGaw presently markets Hespan, an artificial plasma volume expander, and Abbott and Baxter International, Inc. manufacture and sell a generic equivalent of Hespan.

There also is a risk that BioTime's competitors may succeed in developing safer or more effective products that could render BioTime's products and technologies obsolete or noncompetitive.

*BioTime Will Spend a Substantial Amount of Capital on Research and Development But Might Not Succeed in Developing Products and Technologies That Are Useful In Medicine.*

BioTime is attempting to develop new medical products and technologies.

Many of BioTime's experimental products and technologies have not been applied in human medicine and have only been used in laboratory studies on animals. These new products and technologies might not prove to be safe and efficacious in the human medical applications for which they were developed.

The experimentation that the Company is doing is costly, time consuming and uncertain as to its results. BioTime spent \$1,103,490 on research and development during 2002, and \$22,734,008 in total from BioTime's inception on November 30, 1990 through December 31, 2002.

If BioTime is successful in developing a new technology or product, refinement of the new technology or product and definition of the practical applications and limitations of the technology or product may take years and require the expenditure of large sums of money. For example, BioTime spent approximately \$5,000,000 on research and development of Hextend before commencing clinical trials on humans during October 1996. The cost of completing the Hextend clinical trials and preparing an FDA application was approximately \$3,000,000. These costs exclude corporate overhead included in general and administrative costs in the Company's financial statements.

Future clinical trials of new products such as PentaLyte may take longer and may be more costly than BioTime's Hextend clinical trials. The FDA permitted the Company to proceed directly into a Phase III clinical trial of Hextend involving only 120 patients because the active ingredients in Hextend had already been approved for use by the FDA in other products. Because PentaLyte contains a starch that has not been approved by the FDA for use in a plasma volume expander, the Company had to complete a Phase I clinical trial of PentaLyte, and may have to complete a Phase II clinical trial in addition to a Phase III trial, or a combined Phase II/Phase III trial, that will involve more patients than the Hextend trials. BioTime does not yet know the scope or cost of the clinical trials that the FDA will require for PentaLyte or the other products BioTime is developing.

*The Company Has Incurred Operating Losses Since Inception and Does Not Know If It Will Attain Profitability*

From November 1990, the date BioTime was incorporated, through December 31, 2002 the Company incurred \$33,615,170 of cumulative losses. BioTime's net losses for the fiscal years ended December 31, 2000, 2001 and 2002 were \$4,925,024, \$3,658,825 and \$2,844,932, respectively. BioTime's ability to generate sufficient operating revenue to earn a profit depends upon its success in developing and marketing or licensing its products and technology for medical use.



*BioTime Might Not Be Able To Raise Additional Capital Needed To Pay Operating Expenses*

BioTime plans to continue to incur substantial research, product development, and regulatory expenses, and will need to raise additional capital to pay operating expenses until it is able to generate sufficient revenues from product sales, royalties, and license fees. BioTime has not received an amount of royalties and licensing fees from the sale of Hextend sufficient to cover operating expenses. As of December 31, 2002, BioTime had \$1,284,432 of cash and cash equivalents on hand. At the current rate of spending, those funds will last approximately 15 months. The amount and pace of research and development work that the Company can do or sponsor, and the Company's ability to commence and complete clinical trials required to obtain FDA and foreign regulatory approval of products, depends upon the amount of money the Company has. Future research costs are not presently determinable due to many factors, including the inherent uncertainty of those costs and the uncertainty as to the timing, source, and amount of capital that will become available for those projects. BioTime has already curtailed the pace of its product development efforts due to the limited amount of funds available. Further laboratory and clinical studies may have to be postponed, unless the Company's cash resources increase through a growth in revenues or additional equity investment or borrowing. In addition, BioTime must repay \$3,350,000 of debenture indebtedness by August 2004. Although the Company will continue to seek licensing fees from pharmaceutical companies for licenses to manufacture and market its products abroad, it is likely that additional sales of equity or debt securities will be required to meet short-term capital needs and to pay the debenture indebtedness. Sales of additional equity securities could result in the dilution of the interests of present shareholders. The Company may not be able to raise a sufficient amount of additional funds to permit the development and marketing of BioTime products. Unless BioTime is able to generate sufficient revenue or raise additional funds when needed, it is likely that it will be unable to continue its planned activities, even if it is making progress with its research and development projects.

*If BioTime is Unable To Enter Into Additional Licensing Or Manufacturing Arrangements, It May Have to Incur Significant Expense To Acquire Manufacturing Facilities And A Marketing Organization*

The Company presently does not have adequate facilities or resources to manufacture its products and the ingredients used in its products. The Company plans to enter into arrangements with pharmaceutical companies for the production and marketing of BioTime products. BioTime has granted Abbott an exclusive license to manufacture and market Hextend in the United States and Canada, and has granted CJ a license to manufacture and market Hextend and PentaLyte in South Korea. Although a number of pharmaceutical companies have expressed their interest in obtaining licenses to manufacture and market BioTime products in other countries, BioTime might not be successful in negotiating other licensing arrangements. If licensing or manufacturing arrangements cannot be made on acceptable terms, BioTime will have to construct or acquire its own manufacturing facilities and establish its own marketing organization, which would entail significant expenditures of time and money.

*BioTime's Business Could Be Adversely Affected If It Loses the Services Of The Key Personnel Upon Whom It Depends*

The Company depends to a considerable degree on the continued services of executive officers, especially Paul Segall, its Chief Executive Officer. BioTime has \$1,000,000 of key man insurance on Dr. Segall but not on any other executive officer. The loss of the services of any of the executive officers could have a material adverse effect on us. BioTime does not presently have long term employment agreements with any of its executive officers because its present financial situation precludes making long term compensation commitments in amounts commensurate with prevailing salaries of executive officers of similar companies in the San Francisco Bay Area. In addition, BioTime's success will depend, among other factors, upon successful recruitment and retention of additional highly skilled and experienced management and technical personnel.

**Risks Related to BioTime's Industry**

The Company will face certain risks arising from regulatory, legal, and economic factors that affect its business and the business of other pharmaceutical development companies. Because BioTime is a small company with limited revenues and limited capital resources, it may be less able to bear the financial impact of these risks than larger companies that have substantial income and available capital.

*If BioTime Does Not Receive FDA and Other Regulatory Approvals It Will Not Be Permitted To Sell Its Products*

The products that the Company develops cannot be sold until the FDA and corresponding foreign regulatory authorities approve the products for medical use. BioTime has received FDA and Canadian approvals to market Hextend in the United States and Canada only. A Phase I clinical trial of PentaLyte has been completed that provided data concerning the safety of PentaLyte, but BioTime does not presently have sufficient funds for the Phase II or later stage clinical trials that will be necessary to demonstrate that PentaLyte can be used safely and effectively as a plasma volume expander in surgery.

The need to obtain regulatory approval to market a new product means that:

BioTime will have to conduct expensive and time consuming clinical trials of new products.

BioTime will incur the expense and delay inherent in seeking FDA and foreign regulatory approval of new products. For example, 12 months elapsed between the date BioTime filed an application to market Hextend and the date on which the application was approved. Approximately 36 months elapsed between the date BioTime filed an application for approval to market Hextend in Canada, and the date on which the application was approved, even though BioTime did not have to conduct any additional clinical trials. BioTime also has an application pending in Sweden to market Hextend

there. BioTime filed that application during August 2000 and BioTime responded to the latest request for information by the Swedish authorities in August 2002.

A product that is approved may be subject to restrictions on use.

The FDA can recall or withdraw approval of a product if problems arise.

BioTime will face similar regulatory issues in foreign countries.

*BioTime's Patents May Not Protect Its Products From Competition*

BioTime has patents in the United States, Canada, the European Union countries, Australia, Israel, Russia, Hong Kong, South Africa, Japan, South Korea, and Singapore, and has filed patent applications in other foreign countries, for certain products, including Hextend, HetaCool, and PentaLyte. BioTime might not be able to obtain any additional patents, and any patents that it obtains might not be comprehensive enough to provide meaningful patent protection. Also, there will always be a risk that competitors might be able to successfully challenge the validity or enforceability of any patent issued. The costs required to uphold the validity and prevent infringement of any patent could be substantial, and BioTime might not have the resources available to defend its patent rights.

*The Price and Sale of BioTime's Products May Be Limited By Health Insurance Coverage And Government Regulation*

Success in selling BioTime's products may depend in part on the extent to which health insurance companies, HMOs, and government health administration authorities such as Medicare and Medicaid will pay for the cost of the products and related treatment. Presently, most health insurance plans and HMOs will pay for Hextend when it is used in a surgical procedure that is covered by the plan. However, until BioTime actually introduces a new product into the medical market place it will not know with certainty whether adequate health insurance, HMO, and government coverage will be available to permit the product to be sold at a price high enough to generate a profit. In some foreign countries, pricing or profitability of health care products is subject to government control which may result in low prices for BioTime's products. In the United States, there have been a number of federal and state proposals to implement similar government controls, and new proposals are likely to be made in the future.

**Risks Pertaining to BioTime's Common Shares**

*Because BioTime is a Drug Development Company, The Price Of BioTime's Stock May Rise And Fall Rapidly*

The market price of BioTime shares, like that of the common stock of many biotechnology companies, has been highly volatile. The price of BioTime shares may rise rapidly in response to certain events, such as the commencement of clinical trials of an experimental new drug, even though the outcome of those trials and the likelihood of ultimate FDA approval remains uncertain. Similarly, prices of BioTime shares may fall rapidly in response to certain events such as unfavorable results of clinical trials or a delay or failure to obtain FDA approval. The failure of BioTime's earnings to meet analysts' expectations could result in a significant rapid decline in the market price of BioTime's common shares. In addition, the stock market has experienced and continues to experience extreme price and volume fluctuations which have affected the market price of the equity securities of many biotechnology companies and which have often been unrelated to the operating performance of these companies. Broad market fluctuations, as well as general economic and political conditions, may adversely affect the market price of the common shares.

*Because BioTime Does Not Pay Dividends, BioTime's Stock May Not Be A Suitable Investment For Anyone Who Needs To Earn Dividend Income*

BioTime does not pay cash dividends on its common shares. For the foreseeable future BioTime anticipates that any earnings generated in its business will be used to finance the growth of the Company and will not be paid out as dividends to shareholders. BioTime has also agreed not to declare or pay any cash dividends on its capital stock or to redeem or repurchase any shares of its capital stock, until it has paid off its \$3,350,000 of debenture indebtedness in full with interest. This means that BioTime's stock may not be a suitable investment for anyone who needs to earn income from their investments.

## **Item 2. Facilities.**

The Company occupies its office and laboratory facility in Berkeley, California under a lease that will expire on March 31, 2004. The Company presently occupies approximately 8,890 square feet of space and pays rent in the amount of \$11,355 per month. The rent will increase annually by the greater of 3% and the increase in the local consumer price index, subject to a maximum annual increase of 7%. The Company also pays all charges for utilities and garbage collection.

The Company has an option to extend the term of the lease for a period of three years, and to terminate the lease early upon six months notice.

The Company uses, on a fee per use basis, facilities for surgical research on animals at an unaffiliated privately run research center located in Winters, California. Contracting for the use of research facilities has enabled the Company to initiate its research projects without the substantial capital cost, overhead costs and delay associated with the acquisition and maintenance of a modern animal surgical research facility.

**Item 3. Legal Proceedings.**

The Company is not presently involved in any material litigation or proceedings, and to the Company's knowledge no such litigation or proceedings are contemplated.

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

The Company held its annual meeting of shareholders on October 28, 2002. At the meeting, the shareholders elected directors and voted to approve the Company's 2002 Stock Option Plan and to ratify the appointment of the Company's independent auditors.

The following table presents the results of the vote for the election of directors.

<u>Director</u>	<u>Votes For</u>	<u>Votes Withheld</u>
Milton H. Dresner	11,968,619	215,723
Katherine Gordon	11,968,619	215,723
Jeffrey B. Nickel	11,915,719	268,623
Judith Segall	11,944,789	239,553
Paul Segall	11,850,609	333,733
Hal Sternberg	11,915,719	268,623
Harold Waitz	11,968,619	215,723
Michael D. West	11,968,619	215,723

There were 5,580,171 votes for the approval of the 2002 Stock Option Plan, 535,891 votes against, and 6,068,280 abstentions and broker non-votes.

There were 11,846,493 votes for the ratification of the appointment of Deloitte & Touche, the Company's independent auditors, 153,297 votes against, and 184,552 abstentions.

**Part II****Item 5. Market for Registrant's Common Equity and Related Stockholder Matters.**

The Company's Common Shares have been trading on the American Stock Exchange since August 31, 1999, and traded on the Nasdaq National Market from April 28, 1998 to August 30, 1999, and on the Nasdaq SmallCap Market from March 5, 1992 through April 27, 1998. The closing price of the Company's Common Shares on the AMEX on March 27, 2003 was \$1.60.

The following table sets forth the range of high and low bid prices for the Common Shares for the fiscal years ended December 31, 2001 and 2002 based on transaction data as reported by the AMEX.

<u>Quarter Ended</u>	<u>High</u>	<u>Low</u>
March 31, 2001	11.10	6.23
June 30, 2001	8.50	6.40
September 30, 2001	7.95	4.50
December 31, 2001	6.15	4.22
March 31, 2002	4.70	3.00
June 30, 2002	3.10	2.15
September 30, 2002	2.20	1.10
December 31, 2002	1.90	0.85

As of March 20, 2003, there were 385 shareholders of record of the Common Shares based upon information from the Registrar and Transfer Agent.

The Company has paid no dividends on its Common Shares since its inception and does not plan to pay dividends on its Common Shares in the foreseeable future. BioTime has also agreed not to declare or pay any cash dividends on its capital stock or to redeem or repurchase any shares of its capital stock, until it has paid off in full the indebtedness on certain debentures issued during August 2001. See Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources.

**Securities Authorized For Issuance Under Equity Compensation Plans**

The following table shows certain information concerning the options outstanding and available for issuance under the 1992 and 2002 Stock Option Plans as of December 31, 2002. The Company had no other equity compensation plans in effect.

**Equity Compensation Plan Information**

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options (a)	Weighted-Average Exercise Price of Outstanding Options (b)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c)
Equity Compensation Plans Approved by Shareholders	835,033	\$ 5.38	536,668

**Item 6. Selected Financial Data.**

The selected financial data as of, and for the periods ended, December 31, 2002, 2001, 2000, 1999 and 1998, and June 30, 1998 presented below have been derived from the audited financial statements of the Company. The selected financial data should be read in conjunction with the Company's financial statements and notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere herein.

**Statement of Operations Data:**

	Year Ended December 31,				Six Months Ended December 31,	Year Ended June 30,
	2002	2001	2000	1999	1998	1998
<b>REVENUE:</b>						
License fee	\$	\$	\$	\$ 1,037,500	\$ 250,000	\$ 1,150,000
Royalty from product sales	352,641	151,917	52,492			
Reimbursed regulatory fees	34,379					
<b>Total revenue</b>	<b>387,020</b>	<b>151,917</b>	<b>52,492</b>	<b>1,037,500</b>	<b>250,000</b>	<b>1,150,000</b>
<b>EXPENSES:</b>						
Research and development	(1,103,490)	(1,685,168)	(3,362,841)	(4,900,521)	(1,723,860)	(3,048,775)
General and administrative	(1,318,159)	(1,961,342)	(1,779,931)	(1,896,690)	(710,131)	(1,849,312)
<b>Total expenses</b>	<b>(2,421,649)</b>	<b>(3,646,510)</b>	<b>(5,142,772)</b>	<b>(6,797,211)</b>	<b>(2,433,991)</b>	<b>(4,898,087)</b>
<b>INTEREST EXPENSE AND OTHER INCOME:</b>						
Interest expense	(830,952)	(278,576)				
Other income	20,649	114,344	165,256	279,827	89,513	294,741
<b>Total interest expense and other income</b>	<b>(810,303)</b>	<b>(164,232)</b>	<b>165,256</b>	<b>279,827</b>	<b>89,513</b>	<b>294,741</b>
<b>NET LOSS</b>	<b>\$ (2,844,932)</b>	<b>\$ (3,658,825)</b>	<b>\$ (4,925,024)</b>	<b>\$ (5,479,884)</b>	<b>\$ (2,094,478)</b>	<b>\$ (3,453,346)</b>
<b>BASIC AND DILUTED LOSS PER SHARE</b>						
	\$ (0.23)	\$ (0.32)	\$ (0.44)	\$ (0.51)	\$ (0.21)	\$ (0.35)
<b>COMMON AND EQUIVALENT SHARES USED IN COMPUTING PER SHARE AMOUNTS:</b>						
<b>BASIC AND DILUTED</b>	<b>12,368,466</b>	<b>11,562,108</b>	<b>11,042,087</b>	<b>10,688,100</b>	<b>10,008,468</b>	<b>9,833,156</b>



	December 31, 2002	December 31, 2001	December 31, 2000	December 31, 1999	December 31, 1998	June 30, 1998
<b>Balance Sheet Data:</b>						
Cash, cash equivalents and short term investments	\$1,284,432	\$1,652,748	\$1,318,338	\$5,292,806	\$2,429,014	\$4,105,781
Working Capital	883,695	1,452,832	1,081,237	4,804,579	2,157,578	3,724,663

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	December 31, 2002	December 31, 2001	December 31, 2000	December 31, 1999	December 31, 1998	June 30, 1998
Total assets	1,496,081	1,941,375	1,677,484	5,678,644	2,809,455	4,641,780
Debtures, net of discount	2,168,804	1,731,122				
Shareholders' equity (deficit)	(1,171,146)	(99,094)	1,317,735	5,083,132	2,384,752	4,014,750

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

**Overview**

Since its inception in November 1990, the Company has been engaged primarily in research and development activities which have culminated in the commercial launch of Hextend, its lead product, and a clinical trial of PentaLyte. The Company's operating revenues have been generated primarily from licensing fees, including \$2,500,000 received from Abbott Laboratories from April, 1997 through December, 1999 for the right to manufacture and market Hextend® in the United States and Canada. As a result of the developmental nature of its business and the limited sales of its product, since the Company's inception in November 1990 it has incurred \$33,615,170 of losses. The Company's ability to generate substantial operating revenue depends upon its success in developing and marketing or licensing its plasma volume expanders and organ preservation solutions and technology for medical use.

Most of the Company's research and development efforts have been devoted to the Company's first three blood volume replacement products: Hextend,® PentaLyte,® and HetaCool. By testing and bringing all three products to the market, BioTime can increase its market share by providing the medical community with solutions to match patients' needs. By developing technology for the use of HetaCool in low temperature surgery, trauma care, and organ transplant surgery, BioTime may also create new market segments for its product line.

The Company's first product, Hextend, is a physiologically balanced blood plasma volume expander, for the treatment of hypovolemia. Hextend is being sold in the United States by Abbott Laboratories under an exclusive license from the Company. Abbott has the right to sell Hextend in Canada, where it has been approved, and product launch is imminent. Abbott also has a right to obtain licenses to manufacture and sell other BioTime products.

Under its License Agreement with the Company, Abbott will report sales of Hextend and pay the Company the royalties and license fees due on account of such sales within 90 days after the end of each calendar quarter. The Company recognizes such revenues in the quarter in which the sales report is received, rather than the quarter in which the sales took place, as the Company does not have sufficient sales history to accurately predict quarterly sales. Hextend sales are still in the ramp-up phase.

Royalties on sales that occurred during the fourth quarter of 2001 through the third quarter of 2002 are reflected in the Company's financial statements as revenue for the year ended December 31, 2002. Revenues for the year ended December 31, 2002 were \$387,020. The following graph illustrates annual Hextend revenues derived from quarterly royalty payment reports from Abbott. Revenues from Hextend are still in the ramp-up phase, as illustrated by the graph:

Royalties of \$96,622 on sales that occurred during the fourth quarter of 2002 will be reflected in the Company's financial statements for the first quarter of 2003. The following graph illustrates the rise of Hextend revenues on sales during the fourth quarter recognized as revenues during the first quarter of each year since 2000:

As shown above, revenues from Hextend increased progressively from year to year. BioTime attributes these gains in revenues to escalating marketing efforts, an accelerating demand for Hextend by physicians and hospitals due to its outstanding performance in many hundreds of operating rooms around the country, recent clinical trial results which highlight its many clinical benefits, the dissemination of information in the medical literature about the FDA Blood Products Advisory Committee recommendation to add a warning label to a competitive product, and its purchase by the United States Armed Forces for the treatment of combat casualties.

Hextend has become the standard plasma volume expander at a number of prominent teaching hospitals and leading medical centers. BioTime believes that as Hextend use proliferates within the leading US hospitals, other smaller hospitals will follow their lead and accelerate sales growth. Hextend is used overseas by the United States Armed Forces, and has been designated the volume expander of choice as the primary fluid for military pre-hospital hypotensive resuscitation by the United States Army Medical Department in their algorithm for combat fluid resuscitation.

The Company has completed a Phase I clinical trial of PentaLyte and is planning the next phase of its clinical trials in which PentaLyte will be used to treat hypovolemia in surgery. BioTime has spent approximately \$2,000,000 in direct costs through December 31, 2002 developing PentaLyte. The Company's ability to commence and complete additional clinical studies of PentaLyte depends on its cash resources and the costs involved, which are not presently determinable. Clinical trials of PentaLyte in the United States may take longer and may be more costly than the Hextend clinical trials, which cost approximately \$3,000,000. The FDA permitted the Company to proceed directly into a Phase III clinical trial of Hextend involving only 120 patients because the active ingredients in Hextend had already been approved for use in plasma expanders by the FDA in other products. Because PentaLyte contains a starch (pentastarch) that has not been approved by the FDA for use in a plasma volume expander (although pentastarch is approved in the US for use in certain intravenous solutions used to collect certain blood cell fractions), the Company had to complete a Phase I clinical trial of PentaLyte, and may have to complete a Phase II clinical trial in addition to a Phase III trial or a combined Phase II/III trial, that will involve more patients than the Hextend trials. The Company estimates that the Phase II trial that it is planning could be undertaken for approximately \$1,500,000, but it does not know yet the actual scope or cost of the clinical trials that the FDA will require for PentaLyte or the other products BioTime is developing.

Plasma volume expanders containing pentastarch have been approved for use in certain foreign countries including Canada and those of the European Union and Japan. The regulatory agencies in those countries may be more willing to accept applications for regulatory approval of PentaLyte based upon clinical trials smaller in scope than those that may be required by the FDA. This would permit BioTime to bring PentaLyte to market overseas more quickly than in the United States, provided that suitable licensing arrangements can be made with multinational or foreign pharmaceutical companies to obtain financing for clinical trials and manufacturing and marketing arrangements.

The Company is also continuing to develop solutions for low temperature surgery. Once a sufficient amount of data from successful low temperature surgery has been compiled, the Company plans to seek permission to use Hextend as a complete replacement for blood under near-freezing conditions. BioTime currently plans to market Hextend for complete blood volume replacement at very low temperatures under the registered trade mark HetaCool after FDA approval is obtained.

In February, 2001, BioTime launched a research program using HetaCool in animal models of trauma at the State University of New York Health Science Center in Brooklyn. Preliminary laboratory results there have already supported the feasibility of using HetaCool to treat subjects following severe hemorrhage. The use of HetaCool at near-freezing temperatures also will be studied

in animal models of cardiovascular surgery at the Texas Heart Institute in Houston. The project has been approved by the appropriate internal committees, and is awaiting the beginning of experimentation.

BioTime has spent approximately \$1,600,000 through December 31, 2002 developing HetaCool, including about \$25,000 spent during the three months ended December 31, 2002. These costs do not include the cost of developing Hextend, upon which HetaCool is based. BioTime scientists believe the the HetaCool program has the potential to produce a product that could be used in very high fluid volumes (50 liters or more per procedure if HetaCool were used as an multi-organ donor preservation solution or to temporarily replace substantially all of the patient's circulating blood volume) in cardiovascular surgery, trauma treatment, and organ transplantation. However, the cost and time to complete the development of HetaCool, including clinical trials, cannot presently be determined.

Until such time as BioTime is able to complete the development of PentaLyte and HetaCool and enter into commercial license agreements for those products and foreign commercial license agreements for Hextend, BioTime will depend upon royalties from the sale of Hextend by Abbott Laboratories as its principal source of revenues.

Abbott has an option to obtain a license to market PentaLyte and HetaCool in the United States and Canada, and BioTime would receive additional license fees if those options are exercised, in addition to royalties on subsequent sales of those products. The Company recently granted to CJ an exclusive license to manufacture and sell Hextend and PentaLyte in South Korea, but CJ will have to obtain Regulatory approvals before sales can begin. BioTime and certain pharmaceutical companies are discussing and negotiating potential manufacturing, distributing and marketing agreements for BioTime products in the rest of the world.

The amount and pace of research and development work that BioTime can do or sponsor, and BioTime's ability to commence and complete clinical trials required to obtain FDA and foreign regulatory approval of products, depends upon the amount of money BioTime has. Future research and clinical study costs are not presently determinable due to many factors, including the inherent uncertainty of these costs and the uncertainty as to timing, source, and amount of capital that will become available for these projects. The Company has already curtailed the pace of its product development efforts due to the limited amount of funds available, and it may have to postpone further laboratory and clinical studies, unless its cash resources increase through growth in revenues, the completion of licensing agreements, additional equity investment, borrowing or third party sponsorship.

Because the Company's research and development expenses, clinical trial expenses, and production and marketing expenses will be charged against earnings for financial reporting purposes, management expects that there will be losses from operations from time to time during the near future.

Hextend® and PentaLyte® are registered trademarks, and HetaCool is a trademark, of BioTime.

## Results of Operations

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### *Year Ended December 31, 2002 and Year Ended December 31, 2001*

For the year ended December 31, 2002, the Company recognized \$352,641 of royalty revenues, compared with \$151,917 recognized for the year ended December 31, 2001. This increase in royalties is attributable to an increase in product sales by Abbott. Under its License Agreement with the Company, Abbott reports sales of Hextend and pays the Company the royalties and license fees due on account of such sales within 90 days after the end of each calendar quarter. The Company recognizes such revenues in the quarter in which the sales report is received, rather than the quarter in which the sales took place, as the Company does not have sufficient sales history to accurately predict quarterly sales. Royalties on sales made during the fourth quarter of 2002 will not be recognized by the Company until the first quarter of fiscal year 2003. The Company also received a reimbursement of \$34,379 from Abbott for regulatory fees incurred by the Company.

For the year ended December 31, 2002, interest and other income decreased to \$20,649 from \$114,344 for the year ended December 31, 2001. The decrease is attributable to lower interest rates and cash balances for 2002, versus 2001.

Research and development expenses decreased to \$1,103,490 for the year ended December 31, 2002, down from \$1,685,168 for the year ended December 31, 2001. The decrease is chiefly attributable to a significant decrease in fees paid to scientific consultants of \$257,118, a decrease in expenses for laboratory equipment of \$10,293, and a decrease in research and development salaries of \$226,219. Research and development expenses include laboratory study expenses, European clinical trial expenses, salaries, preparation of additional regulatory applications in the United States and Europe, manufacturing of solution for trials, and consultants' fees. It is expected that research and development expenses will increase if the Company obtains sufficient capital to commence new clinical studies of its products in the United States and Europe.

General and administrative expenses decreased to \$1,318,159 for the year ended December 31, 2002 from \$1,961,342 for the year ended December 31, 2001. This decrease is chiefly attributable to a significant decrease in expenditures for the Company's Annual Report and Meeting of \$155,438, a decrease in general and administrative consulting of \$29,252, a decrease in investor/public relations of \$23,420, a decrease in meeting costs of \$21,332, a decrease in spending for office supplies and expenses of \$17,760, a decrease in telephone expenses of \$15,347, a decrease in travel expenses of \$12,966, and a decrease in general and administrative salaries of \$197,448.

The company's interest expense increased by \$552,376 during 2002 because the Company incurred interest expense related to its debentures for all of 2002, whereas the Company only incurred approximately five months of interest expense during 2001 in relation to the debentures, which were executed in August 2001.

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*Year Ended December 31, 2001 and Year Ended December 31, 2000*

For the year ended December 31, 2001, the Company recognized \$151,917 of royalty revenues. Under its License Agreement with the Company, Abbott reports sales of Hextend and pays the Company the royalties and license fees due on account of such sales within 90 days after the end of each calendar quarter. The Company recognizes such revenues in the quarter in which the sales report is received, rather than the quarter in which the sales took place, as the Company does not have sufficient sales history to accurately predict quarterly sales. Royalties on sales made during the fourth quarter of 2001 will not be recognized by the Company until the first quarter of fiscal year 2002.

For the year ended December 31, 2001, interest and other income decreased to \$114,344 from \$165,256 for the year ended December 31, 2000. The decrease is attributable to lower interest rates and cash balances for 2001, versus 2000.

Research and development expenses decreased to \$1,685,168 for the year ended December 31, 2001, down from \$3,362,841 for the year ended December 31, 2000. The decrease is attributable to a significant decrease in laboratory study expenses and fees paid to scientific research personnel as a result of a cost reduction program in which the Company reduced its research and development activities: in total, in 2001, the Company spent \$9,310 less than it had in the prior year for laboratory supplies, \$107,109 less for laboratory expenses, \$278,107 less for salaries related to research and development, and \$256,028 less for scientific consulting fees. Research and development expenses include laboratory study expenses, European clinical trial expenses, salaries, preparation of additional regulatory applications in the United States and Europe, manufacturing of solution for trials, and consultants' fees. It is expected that research and development expenses will increase if the Company obtains sufficient capital to commence new clinical studies of its products in the United States and Europe.

General and administrative expenses increased to \$1,961,342 for the year ended December 31, 2001 from \$1,779,931 for the year ended December 31, 2000. This increase is attributable to an increase in expenditures for the Company's Annual Report and Meeting of \$25,347, an increase in fees required for continued stock exchange listing of \$12,882, an increase in overall insurance costs of \$39,277, an increase in investor/public relations costs of \$41,147, an increase in legal and accounting fees of \$74,996, and an increase in costs associated with continued maintenance of the Company's patent portfolio in the amount of \$129,289. Increases were offset to some extent by an overall decrease in general and administrative salaries of \$108,044.

The company's interest expense increased by \$278,576 during 2001 because it began to borrow money to meet its capital needs.



## Taxes

At December 31, 2002 the Company had a cumulative net operating loss (NOL) carryforward of approximately \$39,865,000 for federal income tax purposes. The gross deferred tax asset of \$15,944,000 is principally related to the available benefit from NOL carryforwards and tax credit carryforwards. Because of the Company's history of operating losses, the deferred tax asset has been fully reserved at December 31, 2002 and 2001. Utilization of the NOL and tax credit carryforwards may be limited in the event of certain ownership changes. Refer to Note 7 to the Financial Statements.

## Liquidity and Capital Resources

As of December 31, 2002, the Company had \$1,284,432 of cash and cash equivalents on hand. At the current rate of spending, the Company estimates that those funds will last approximately 15 months.

Since inception, the Company has primarily financed its operations through the sale of equity securities, licensing fees, royalties, and borrowings. On March 27, 2003, the Company entered into the CJ Agreement and expects to receive the initial \$500,000 license fee payment within 30 days. A second installment of \$300,000 will be payable by CJ 30 days after its submits an application for regulatory approval of Hextend. On August 12, 2002, BioTime completed a private placement of 1,852,785 common shares for \$2,075,119 (\$1,764,670 net proceeds after cash placement fees of \$310,449) through Ladenburg Thalmann & Co. Inc. The Company has registered these shares for sale under the Securities Act of 1933, as amended. In connection with the offering, and in addition to the placement fees referred to above, the Company granted to Ladenburg Thalmann & Co. Inc., warrants to purchase 129,695 common shares at an exercise price of \$1.34 per share. The warrants are fully vested and non-forfeitable, and expire on August 11, 2007.

During August 2001, the Company received cash and converted debt totaling \$3,350,000 through the sale of debentures to a group of private investors, including Alfred D. Kingsley, an investor and consultant to the Company, who purchased \$1,500,000 of debentures, and Milton Dresner, a director of the Company. Mr. Kingsley's investment included the conversion of the \$1,000,000 principal balance of a line of credit that he had previously provided.

Interest on the debentures is payable at an annual rate of 10% and is payable semiannually. The principal amount of the debentures will be due and payable on August 1, 2004. BioTime may prepay the debentures, in whole or in part, at any time without premium or penalty. Under the terms of the debentures BioTime has agreed to restrict its quarterly cash payments for operating expenses to not more than \$450,000 (excluding interest payable on the debentures) plus the amount of cash revenues (excluding interest and dividends) it collects for the quarter. To the extent BioTime's expenditures during any quarter are less than \$450,000 over its revenues, it may expend the difference in one or more subsequent quarters. The spending restriction will expire when BioTime obtains at least \$5,000,000 in cash through sales of equity securities or pays off the debenture indebtedness in full. For this purpose, cash revenues will include royalties, license fees, and other proceeds from the sale or licensing of its products and technology, but will not include interest, dividends, and any monies borrowed or the proceeds from the issue or sale of any debt or equity securities. BioTime has also agreed not to declare or pay any cash dividends on its capital stock or to redeem or repurchase any shares of its capital stock, until it has paid off the debenture indebtedness in full.

During April 2003, holders of \$2,750,000 principal amount of the Debentures granted BioTime a "pay in kind" right allowing (but not requiring) BioTime to make interest payments in common shares instead of cash for the interest payments due during August 2003 and February 2004 (the "PIK Right"). BioTime retained the right to pay the interest due in cash.

Each debenture holder who agreed to grant BioTime the PIK Right received a three-year warrant entitling the holder to purchase BioTime common shares for \$1.50 per share. The number of shares covered by the warrants is the amount of debenture interest due in August 2003 and February 2004 divided by the \$1.50 exercise price. Warrants to purchase a total of 223,331 common shares were issued.

The warrants will expire in three years and will not be exercisable thereafter. The warrants will be redeemable by BioTime at \$0.05 per warrant share if the closing price of the common shares on the American Stock Exchange exceeds 200% of the exercise price for 20 consecutive trading days.

If BioTime actually elects to pay interest in stock instead of cash, the common shares issued on the interest payment date will be valued at the lower of (a) \$1.20 or (b) 80% of the average closing price of BioTime common shares on the AMEX for the 10 trading days prior to the interest payment date, but not less than \$0.80 per share.

BioTime granted registration rights for the warrants and shares on substantially the same terms as the registration rights covering the warrants issued when the debentures were originally sold. All prices and share amounts will be adjusted for any stock splits, reverse splits, recapitalization, or similar changes to the common shares.

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Alfred Kingsley has agreed with BioTime that if BioTime exercises the PIK right he will provide BioTime with the cash required to pay the interest due on \$600,000 principal amount of debentures held by persons who did not grant BioTime the PIK Right. In consideration of his agreement to do so, BioTime will issue to Mr. Kingsley a warrant for 39,999 additional common shares, which is the number of shares that would have been issued had those debenture holders agreed to grant the PIK Right. When Mr. Kingsley provides BioTime with the cash to pay the interest due, he will receive the number of shares that the debenture holders would have received had they accepted stock in lieu of cash interest payments.

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In August 2001, investors who purchased the debentures also received warrants to purchase a total of 515,383 common shares at an exercise price of \$6.50 per share. The warrants will expire if not exercised by August 1, 2004. Since the end of June 2002, the Company has had the right to call the warrants for redemption at a redemption price of \$0.01 per share if the closing price of the Company's common shares on the American Stock Exchange equals or exceeds 150% of the exercise price for fifteen (15) consecutive trading days and the shares issuable upon the exercise of the warrants have been registered for sale under the Securities Act of 1933, as amended.

On March 27, 2002, the Company entered into a new Credit Agreement with Alfred D. Kingsley under which the Company may borrow up to \$300,000 for working capital purposes. This line of credit has expired, and no amounts were borrowed under it.

In connection with entering into the 2002 Credit Agreement on March 27, 2002, the Company issued to Mr. Kingsley warrants to purchase 30,000 shares of the Company's common stock at \$4.00 per share. The warrants are fully exercisable and non-forfeitable on the date of grant and expire on March 26, 2007. The fair value of the warrant was \$60,390 and was determined using the Black-Scholes option pricing model with the following assumptions: contractual life of 5 years; risk-free interest rate of 4.4%; volatility of 84.6%; and no dividends during the expected term. The fair value of the warrant was included in other current assets at September 30, 2002, and was being amortized over the term of the 2002 Credit Agreement. As the 2002 Credit Agreement expired, the warrant has been fully expensed at September 30, 2002.

BioTime will need to obtain additional equity capital from time to time in the future, as long as the fees it receives from licensing its products to pharmaceutical companies, profits from sales of its products, and royalty revenues are not sufficient to fund its operations. Sales of additional equity securities could result in the dilution of the interests of present shareholders. The amount of license fees and royalties that may be earned through the licensing and sale of the Company's products and technology, the timing of the receipt of license fee payments, and the future availability and terms of equity financing, are uncertain. The unavailability or inadequacy of financing or revenues to meet future capital needs could force the Company to modify, curtail, delay, suspend, or possibly discontinue some or all aspects of its planned operations. If necessary, the Company can reduce costs by downsizing its operations. Management believes its existing cash together with anticipated license fees from CJ Corp. and royalties from Abbott is sufficient to allow the Company to operate at a reduced level through March 31, 2004.

The following depicts BioTime's contractual obligations as of December 31, 2002:

Contractual Obligation	Total	Payments due by Period	
		less than 1 year	1-3 years
Debentures	\$3,350,000	\$	\$3,350,000
Operating Leases	174,000	139,000	35,000
<b>Total Contractual Cash Obligations</b>	<b>\$3,524,000</b>	<b>\$139,000</b>	<b>\$3,385,000</b>

### **Critical Accounting Policies and Estimates**

Management's discussion and analysis of the Company's financial condition and results of operations are based on the Company's financial statements, which have been prepared in conformity with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires management to make judgments and estimates that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. The Company based its estimates on historical experience and on various other assumptions that it believed to be reasonable under the circumstances. Actual results may differ from such estimates under different assumptions or conditions. The following summarizes the Company's critical accounting policies and significant estimates used in preparing its financial statements:

#### *Debenture and Warrant Valuation*

During 2001 and in connection with the issuance of \$3,350,000 of debt, the Company issued warrants to purchase common shares in the Company. The fair value of the warrants was estimated using the Black-Scholes option pricing model and has been recorded at a discount to the debentures. The discount is being amortized using the effective interest rate method over the term of the loan. The Company may prepay the debt, in whole or in part, at any time. If the Company were to prepay the debt, the unamortized portion of the discount would be recognized as a loss on the repayment date.

#### *Revenue Recognition*

Under the Company's License Agreement with Abbott Laboratories, the Company has received \$2,500,000 of license fees from April, 1997 through December, 1999 based upon achievement of specified milestones. Such fees have been recognized as revenue as the milestones were achieved. Up to \$37,500,000 of additional license fees will be payable based upon annual net sales of Hextend, at the rate of 10% of annual net sales if annual net sales exceed \$30,000,000 or 5% if annual net sales are between \$15,000,000 and \$30,000,000. Abbott's obligation to pay licensing fees on sales of Hextend will expire on the earlier of January 1, 2007 or, on a country by country basis, when all patents protecting Hextend in the applicable country expire or any third party obtains certain regulatory approvals to market a generic equivalent product in that country.

In addition to the license fees, Abbott will pay the Company a royalty on total annual net sales of Hextend. The royalty rate will be 5% plus an additional .22% for each \$1,000,000 of annual net sales, up to a maximum royalty rate of 36%. The royalty rate for each year will be applied on a total net sales basis. Abbott's obligation to pay royalties on sales of Hextend will expire in the United States or Canada when all patents protecting Hextend in the applicable country expire and any third party obtains certain regulatory approvals to market a generic equivalent product in that country.

The Company recognizes such revenues in the quarter in which the sales report is received, rather than the quarter in which the sales took place, as the Company does not have sufficient sales history to accurately predict quarterly sales. Revenues for the year ended December 31, 2002 include royalties on sales made by Abbott during the twelve months ended September 30, 2002. Royalties on sales made during the fourth quarter of 2002 will not be recognized by the Company until the first quarter of fiscal year 2003.

*Deferred Tax Asset Valuation Allowance*

The Company records a valuation allowance to reduce its deferred tax assets when it is more likely than not, based upon currently available evidence and other factors, that it will not realize some portion of, or all of, the deferred tax assets. The Company bases its determination of the need for a valuation allowance on an ongoing evaluation of current evidence including, among other things, estimates of future earnings and the expected timing of deferred tax asset reversals. The Company charges or credits adjustments to the valuation allowance to income tax expense in the period in which these determinations are made. If the Company determines that it would be able to realize its deferred tax assets in the future in excess of its net recorded amount, an adjustment to the deferred tax asset would increase income in the period this determination was made. Likewise, if the Company determines that it would not be able to realize all or part of its net deferred tax assets in the future, the Company would charge to operations an adjustment to the deferred tax asset in the period this determination was made.

**Recently Issued Accounting Standards**

See Note 2 to the Financial Statements.

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

The Company did not hold any market risk sensitive instruments as of December 31, 2002, December 31, 2001, or December 31, 2000. The Company's debentures bear interest at a fixed rate of 10% per annum. Changes in interest rates would affect the fair value of the debentures, but such changes would not affect future cash flows.

**REPORT OF INDEPENDENT CERTIFIED PUBLIC ACCOUNTANTS**

Board of Directors and Shareholders  
BioTime, Inc.  
Berkeley, California

We have audited the accompanying consolidated balance sheet of BioTime, Inc. (a development stage company) as of December 31, 2002 and the related consolidated statements of operations, shareholders' equity (deficit), and cash flows for the year then ended. We have also audited the statements of operations, shareholders' equity (deficit), and cash flows for the period from November 30, 1990 (inception) through December 31, 2002, except that we did not audit these financial statements for the period from November 30, 1990 through December 31, 2001; those financial statements were audited by other auditors whose report, which was dated February 16, 2002, expressed an unqualified opinion on those statements. 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 audit.

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. 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 audit provides a reasonable basis for our opinion.

In our opinion, based on our audit and on the report of other auditors, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of BioTime, Inc. at December 31, 2002, and the results of its operations and its cash flows for the year ended December 31, 2002 and for the period from November 30, 1990 (inception) through December 31, 2002, in conformity with accounting principles generally accepted in the United States of America.

The Company is in the development stage as of December 31, 2002. As discussed in Note 1b to the financial statements, successful completion of the Company's product development program and, ultimately, the attainment of profitable operations is dependent upon future events, including maintaining adequate financing to fulfill its development activities, obtaining regulatory approval for products ultimately developed, and achieving a level of revenues adequate to support the Company's cost structure.

/s/BDO SEIDMAN, LLP

San Francisco, California  
March 28, 2003, except for Note 1d which is as of April 4, 2003

INDEPENDENT AUDITORS' REPORT

To the Board of Directors and Shareholders  
BioTime, Inc.:

We have audited the accompanying balance sheet of BioTime, Inc. (a development stage company) as of December 31, 2001, and the related statements of operations, shareholders' equity (deficit) and cash flows for the years ended December 31, 2001 and 2000, and the period from November 30, 1990 (inception) to December 31, 2001. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States of America. 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, such financial statements present fairly, in all material respects, the financial position of BioTime, Inc. as of December 31, 2001, and the results of its operations and its cash flows for the years ended December 31, 2001 and 2000, and the period from November 30, 1990 (inception) to December 31, 2001, in conformity with accounting principles generally accepted in the United States of America.

The Company is in the development stage as of December 31, 2001. As discussed in Note 1 to the financial statements, successful completion of the Company's product development program and, ultimately, the attainment of profitable operations is dependent upon future events, including maintaining adequate financing to fulfill its development activities, obtaining regulatory approval for products ultimately developed, and achieving a level of revenues adequate to support the Company's cost structure.

/s/ DELOITTE & TOUCHE LLP

San Francisco, California  
February 16, 2002



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

**BIOTIME, INC.**  
**(A Development Stage Company)**

**BALANCE SHEETS**

	<b>December 31, 2002</b>	<b>December 31, 2001</b>
	<hr/>	<hr/>
<b>ASSETS</b>		
<b>CURRENT ASSETS</b>		
Cash and cash equivalents	\$ 1,284,432	\$ 1,652,748
Prepaid expenses and other current assets	97,686	109,431
<b>Total current assets</b>	<b>1,382,118</b>	<b>1,762,179</b>

See notes to financial statements.

**BIOTIME, INC.**  
(A Development Stage Company)

**STATEMENTS OF OPERATIONS**

	Year Ended December 31,			Period from Inception (November 30, 1990) to December 31, 2002
	2002	2001	2000	
<b>REVENUE:</b>				
License fee	\$	\$	\$	\$ 2,500,000
Royalty from product sales	352,641	151,917	52,492	557,050
Reimbursed regulatory fees	34,379			34,379
<b>Total revenue</b>	<b>387,020</b>	<b>151,917</b>	<b>52,492</b>	<b>3,091,429</b>
<b>EXPENSES:</b>				
Research and development	(1,103,490)	(1,685,168)	(3,362,841)	(22,734,008)
General and administrative	(1,318,159)	(1,961,342)	(1,779,931)	