BIOTIME INC
Form 10KSB
April 14, 2008

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-KSB

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

For the fiscal year ended December 31, 2007

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.
(Name of small business issuer as specified in its charter)

California	94-3127919
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

6121 Hollis Street
Emeryville, California 94608
(Address of principal executive offices) (Zip Code)

Issuer's telephone number, including area code (510) 350-2940

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

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

Title of class	Common Shares, no par value
Title of class	Common Share Purchase Warrants

Check whether the issuer is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

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

Check if there is no disclosure of delinquent filers pursuant to Item 405 of Regulation S-B contained in this form, and no disclosure will 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-KSB or any amendment to this Form 10-KSB. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act): Yes o No x

The issuer's revenues for the fiscal year ended December 31, 2007 were $1,046,121

The approximate aggregate market value of voting common shares held by nonaffiliates of the issuer computed by reference to the price at which common shares were sold as of March 25, 2007 was $3,517,793. 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.

23,044,374

(Number of common shares outstanding as of March 4, 2008)

Documents Incorporated by Reference

None

Transitional Small Business Disclosure Format (check one): Yes o No x

BioTime, Inc.

Table of Contents

2

Table of Contents

PART I

Statements made in this Form 10-KSB 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 expressio forward-looking statements. See “Risk Factors” and Note 1 to Financial Statements.

Item 1. Description of Business

Overview

Since its inception in November 1990, BioTime has been engaged primarily in research and development activities, which have culminated in the commercial launch of Hextend®, our lead product, and a clinical trial of PentaLyte®. Our operating revenues have been generated primarily from licensing fees and from royalties on the sale of Hextend. During October 2007, we entered the field of regenerative medicine where we plan to develop stem cell related products and technology for diagnostic, therapeutic and research use. Our ability to generate substantial operating revenue depends upon our success in developing and marketing or licensing our plasma volume expanders, stem cell products, and organ preservation solutions and technology for medical and research use.

Products for Stem Cell Research

On October 10, 2007, Michael D. West, Ph.D. became BioTime's new Chief Executive Officer. Dr. West will help spearhead BioTime's entry into the field of regenerative medicine by initiating the development of advanced human stem cell products and technology for diagnostic, therapeutic and research use. Regenerative medicine refers to therapies based on human embryonic stem (“hES”) cell technology that are designed to rebuild cell and tissue function lost due to degenerative disease or injury. To further these ends, in December 2007, BioTime created a new, wholly-owned subsidiary called Embryome Sciences, Inc.™ (“Embryome Sciences”). Human embryonic stem cells are capable of becoming all of the thousands of different cell types in the body. Since embryonic stem cells can now be derived in a noncontroversial manner, they are increasingly likely to be utilized in a wide array of future therapies to restore the function of organs damaged by degenerative diseases such as heart failure, stroke, and diabetes. The future challenge for regenerative medicine is to navigate the complexity of human development and manufacture purified populations of desired cell types. Embryome Sciences represents the merger of new technologies in the field of genomics with the biology of embryonic stem cells to provide scientists with a detailed "roadmap" of the human developmental tree, the factors to push the cells into desired lineages, and tools to purify the desired cell types.

We believe that the development of products in the embryomics sector may allow Embryome Sciences to commercialize products more quickly, using less capital, than developing therapeutic products from stem cells. Embryome Sciences' plan is to market its products and services to companies and academic researchers in this growing industry to provide them with the tools they need to attain their goals.

Table of Contents

The new BioTime subsidiary plans to launch several kinds of research products in the next two years. One such product is a commercial database that will provide the first detailed map of the embryome, thereby aiding researchers in navigating the complexities of human development and in identifying the many hundreds of cell types coming from embryonic stem cells. This map of the human and mouse embryome will take the form of a relational database that would permit researchers to chart the cell lineages of human development, the genes expressed in those cell types, and antigens present on the cell surface of those cells that can be used in purification. The relational database will be built using core software licensed, on an exclusive basis for this purpose, from Targeted Therapeutics Consulting, Inc., which currently operates a relational database for cancer therapy research and the development of anti-cancer drugs. When the new embryome database is operational, Embryome Sciences will provide researchers access to it through an internet website. Embryome Sciences plans to launch this web-based database in the second quarter of 2008. The new website may also be used to market stem cell research products developed by Embryome Sciences and by other companies.

In order to manufacture specific cell types from embryonic stem cells, researchers need to use factors that induce those cells to become a desired cell type. Embryome Sciences plans to develop growth and differentiation factors that can do this, and hopes to launch the first of these products beginning in 2008.

Another category of near-term embryomics products that Embryome Sciences will pursue, to be launched beginning in 2009, is a line of purification tools useful to researchers in quality control of products for regenerative medicine.

We, and our wholly-owned subsidiary Embryome Sciences, Inc., have signed a letter of intent with International Stem Cell Corporation and its wholly-owned subsidiary Lifeline Cell Technology ("Lifeline") to jointly produce and distribute a wide array of research products from human embryonic stem cell technology. Embryome Sciences and Lifeline intend to jointly manufacture products serving the complex needs of this industry, including cells and related products that will allow researchers to identify and study the thousands of cell types that can be made from hES cells. Among these planned products are ESpy TM cell lines (complex derivatives of hES cells that send beacons of light in response to the activation of particular genes). The progenitor cell lines will be produced and distributed in joint efforts utilizing Embryome Science's proprietary "Embryomics™" technology, its future Embryome.com online database, and technology and approved hES cell lines licensed from the Wisconsin Alumni Research Foundation (WARF). Lifeline will contribute its manufacturing and quality control expertise, the use of its facilities, and use of Lifeline's technologies.

The proposed collaboration among Lifeline, BioTime, and Embryome Sciences is subject to the execution of a definitive agreement.

Our ability to commercialize our planned stem cell research products is dependent upon the success of our research and development program, and our ability to obtain the capital needed for the financing of that program.

Plasma Volume Expanders and Related Products

Our 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 helps sustain vital organs during surgery. Hextend, approved for use in major surgery, is the only blood plasma volume expander that contains lactate, multiple electrolytes, glucose, and a medically approved form of starch called hetastarch. Hextend is sterile to avoid risk of infection. Health insurance reimbursements and HMO coverage now include the cost of Hextend used in surgical procedures.

We are also developing two other blood volume replacement products, PentaLyte® and HetaCool®, which, like Hextend, have been formulated to maintain the patient's tissue and organ function by sustaining the patient's fluid volume and physiological balance. We have conducted a Phase II clinical trial using PentaLyte in the treatment of hypovolemia in cardiac 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. Our ability to complete clinical studies of PentaLyte will depend on our cash resources and the costs involved, which are not presently determinable.

Hextend is being distributed in the United States and Canada by Hospira, Inc., and in South Korea by CJ Corp. ("CJ") under exclusive licenses from us. Hospira also has the right to obtain regulatory approval and market Hextend in Latin America and Australia. Summit Pharmaceuticals International Corporation ("Summit") has a license to develop Hextend and PentaLyte in Japan, the People's Republic of China, and Taiwan. Summit has entered into sublicenses with Maruishi Pharmaceutical Co., Ltd. ("Maruishi") to obtain regulatory approval, manufacture, and market Hextend in Japan, and Hextend and PentaLyte in China and Taiwan. See "Licensing" for more information about our licensing arrangements with Hospira, CJ and Summit.

Table of Contents

We are also continuing to develop solutions for low temperature surgery. Once a sufficient amount of data from successful low temperature surgery has been compiled, we plan to seek permission to use Hextend as a complete replacement for blood under near-freezing conditions. We currently plan to market Hextend for complete blood volume replacement at very low temperatures under the registered trademark "HetaCool®" after FDA approval is obtained, although the time frame for such approval is presently uncertain.

BioTime scientists believe 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 a 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 we are able to successfully commercialize any of the various projected regenerative medicine products and can complete the development of PentaLyte and HetaCool and enter into commercial license agreements for those products and additional foreign commercial license agreements for Hextend, we will depend upon royalties from the sale of Hextend by Hospira and CJ as our principal source of revenues.

The amount and pace of research and development work that we can do or sponsor, and our ability to commence and complete clinical trials required to obtain FDA and foreign regulatory approval of products, depends upon the amount of money we have. 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. We have already curtailed the pace of our product development efforts due to the limited amount of funds available, and we may have to postpone further laboratory and clinical studies, unless our cash resources increase through growth in revenues, the completion of licensing agreements, additional equity investment, borrowing or third party sponsorship.

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

The Market for Plasma Volume Expanders

We are 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 low blood pressure due to shock 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 is part of the Tactical Combat Casualty Care protocol and has been purchased by the U.S. Armed Forces through intermittent large volume orders.

Table of Contents

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 his or her 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

More than 400,000 coronary bypass and other open-heart surgeries are performed in the United States each year. Current estimates indicate that more than one million people over age 55 have pathological changes associated with the aortic arch. 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 that 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.

Table of Contents

Uses and Benefits of Hextend, PentaLyte and HetaCool

Our 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. We believe that by testing and bringing these products to the market, we can increase our 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. We expect that PentaLyte will also be able to maintain blood calcium levels and acid-base balance based upon the fact that the electrolyte formulation of PentaLyte is identical to that of Hextend.

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.

We have 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 blood cell count has fallen to the transfusion trigger. Therefore, the lack of oxygen-carrying molecules in BioTime solutions should not pose a significant contraindication to use.

However, our 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.

Table of Contents

Hextend is our 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. We believe 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.

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 clinical trial conducted in 2001, cardiac surgery patients treated with Hextend, maintained more normal kidney function, experienced less pain and nausea, showed less deep venous thrombosis, avoided dialysis, and had shorter delay times to first meal compared to those treated with other fluids.

PentaLyte is our 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 can 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. Our present plan is to seek approval of PentaLyte for use in the treatment of hypovolemia. We have conducted a Phase II clinical study using PentaLyte in cardiac surgery for that purpose.

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 15o and 25o C. However, we are not aware of any fluid currently used in medical practice or any medically approved protocol allowing operations that can completely replace all of a patient's blood at temperatures close to the ice point. We believe 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.

In medical use, 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.

Table of Contents

Hextend has already been used to partially replace blood during cancer surgery in which a patient's body temperature was lowered to 15oC 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 issue of the Canadian Journal of Anesthesia. Hypothermic techniques may also have an important use in treating trauma patients that have experienced severe blood loss. We have conducted a research program using HetaCool in animal models of trauma at the State University of New York Health Science Center in Brooklyn. Laboratory results there have already supported the feasibility of using HetaCool to treat subjects following severe hemorrhage.

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: 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 recipient. 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 recipients may not receive the needed organs.

We are 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. We believe 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

We are 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. We currently estimate that each such preservation procedure could require as much as 50 liters of HetaCool.

Table of Contents

We believe that the ability to replace an animal's blood with HetaCool, 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 human multi-organ preservation. BioTime 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 our 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.

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 our research and development plan. To permit such long-term organ banking we are 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 freeze-protective solutions that may ultimately allow the extension of time during which organs and tissues can be stored for future transplant or surgical grafting. In laboratory experiments, our proprietary freeze-protective compounds have already been used to preserve skin. Silver dollar-sized 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 other 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.

We have also developed a patent pending devise for hyperbaric freezing and thawing of tissues in a manner that might reduce or eliminate structural damage to the cells or tissue samples. This technology may have application in biological and medical research and in the storage of cells and tissues for medical use.

Our scientists have also 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.

Table of Contents

Research and Development Strategy

Plasma Volume Expanders and Organ Preservation Solutions

The greatest portion of our research and development efforts has 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 our research and development efforts have been devoted to developing solutions and protocols for storing organs and tissues at subfreezing temperatures. As the first products achieve market entry, more effort will be expended to bring the next tier of products to maturity.

Experiments intended to test the efficacy of our low temperature blood replacement solutions involve replacing the animal's blood with our solution, maintaining the animal in a cold blood-substituted state for a period of time, and then attempting to revive the animal. An integral part of that effort has been the development of techniques and procedures or "protocols" for use of our products at low temperatures. 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.

We have also done research for the development of products for low temperature preservation of tissues and cells. This area of research includes our work with HetaFreeze and a patent pending device for hyperbaric freezing and thawing of tissues in a manner that might reduce or eliminate structural damage to the cells or tissue samples.

We have been also conducting two collaborative research programs at the University of California at Berkeley. One program is testing our solutions and protocols designed for organ preservation, and the other program is an interventive gerontology project focused on the identification of specific factors central to aging of the brain and the development of medical and pharmacological strategies to treat senescence-related consequences. To date this collaborative research has led to three journal articles. One study, the results of which were published in Neuroendocrinology Letters and in Mechanisms of Aging and Development, demonstrated that a loss of hypothalamic estrogen-binding cells in females may play a role in reproductive aging. The other study, the results of which were published in the International Journal of Developmental Neuroscience in 2007, indicated that the loss of insulin-like Growth Factor Receptor-1 containing cells, within specific hypothalamic areas, may play a key role in aging. As funding permits, we may conduct further research to better understand the cause and effect of these age-related degenerative conditions, and to identify possible therapies that may be developed through the use of hES cell technology.

We intend to continue to foster relations with research hospitals and medical schools for the purpose of conducting collaborative research projects because we believe that such projects will introduce our potential products to members of the medical profession and provide us with objective product evaluations from independent research physicians and surgeons.

Table of Contents

Stem Cell Research Products

In addition to our work with plasma volume expanders and organ preservation solutions, we plan to focus on near-term commercialization opportunities presented by stem cell research programs. We believe that the development of products for use in stem cell research provides an opportunity to commercialize products more quickly, using less capital, than developing therapeutic products. Our plan is to market to companies and academic researchers in the stem cell industry some of the tools they need to attain their goals.

We are conducting our stem cell research product business through our recently organized subsidiary, Embryome Sciences, Inc. We plan to launch several kinds of research products in the next two years. One such product is a commercial embryome database that will provide a map that researchers may use to navigate the complexities of human development and to identify the many hundreds of cell types coming from hES cells. Like the field of "genomics," where companies mapped the human DNA, we believe that there is an important need for a map of the human "embryome" in stem cell research. This map would take the form of a relational data base that would permit researchers to chart the cell lineages of human development, the genes expressed in those cell types, and antigens present on the cell surface of those cells that can be used in purification. We plan to launch this web-based database in the early part of 2008.

We also plan to develop growth and differentiation factors, and hope to launch the first of these products beginning in 2008. In order to manufacture specific cell types from hES cells, researchers need to use factors that signal to hES cells to become a desired cell type. We may market these reagents from a new BioTime website.

Another category of near-term products that we plan to develop includes purification ligands useful to researchers in purification and quality control analysis of products in regenerative medicine. We hope to be able to launch the first of these products in 2009.

We, and our wholly-owned subsidiary Embryome Sciences, Inc., have signed a letter of intent with International Stem Cell Corporation and its wholly-owned subsidiary Lifeline Cell Technology (“Lifeline”) to jointly produce and distribute a wide array of research products from human embryonic stem cell technology. Embryome Sciences and Lifeline intend to jointly manufacture products serving the complex needs of this industry, including cells and related products that will allow researchers to identify and study the thousands of cell types that can be made from hES cells. Among these planned products are ESpy TM cell lines (complex derivatives of hES cells that send beacons of light in response to the activation of particular genes). The progenitor cell lines will be produced and distributed in joint efforts utilizing Embryome Science’s proprietary “Embryomics™” technology, its future Embryome.com online database, and technology and approved hES cell lines licensed from the Wisconsin Alumni Research Foundation (WARF). Lifeline will contribute its manufacturing and quality control expertise, the use of its facilities, and use of Lifeline’s technologies.

The proposed collaboration among Lifeline, BioTime, and Embryome Sciences is subject to the execution of a definitive agreement.

We have obtained a license from the Wisconsin Alumni Research Foundation to use their patented technology and cell lines in our research program. See “Patents and Trade Secrets—Licensed Patents.” We may seek to obtain licenses to additional stem cell technology for use in developing new stem cell products, and we may also enter into collaborative product development arrangements with other companies in the stem cell industry if such opportunities arise on terms acceptable to us.

Licensing

Hospira

Hospira has the exclusive right to manufacture and sell Hextend in the United States, Canada, Latin America and Australia under a license agreement with us. Hospira is presently marketing Hextend in the United States. Hospira's license applies to 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").

Hospira pays us a royalty on total annual net sales of Hextend. The royalty rate is 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 is applied on a total net sales basis. Hospira's obligation to pay royalties on sales of Hextend will expire on a country by country basis 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 relevant composition patents begin to expire in 2014 and the relevant methods of use patents expire in 2019.

Table of Contents

We have the right to convert Hospira's exclusive license to a non-exclusive license or to terminate the license outright if certain minimum sales and royalty payments are not met. In order to terminate the license outright, we would pay a termination fee in an amount ranging from the milestone payments we received to an amount equal to three times prior year net sales, depending upon when termination occurs. Hospira has agreed to manufacture Hextend for sale by us in the event that the exclusive license is terminated.

Hospira has certain rights to acquire additional licenses to manufacture and sell our other plasma expander products in their market territory. If Hospira 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, Hospira will be obligated to pay a license fee based upon our direct and indirect research, development and other costs allocable to the new product. If Hospira desires to acquire a license to sell any of our 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 Hospira will be aggregated with sales of Hextend. If Hospira does not exercise its right to acquire a new product license, we may manufacture and sell the product ourselves or we may license others to do so.

Hospira supplied us with batches of PentaLyte for our clinical trial, and performed characterization and stability studies, and other regulatory support needed for our clinical studies. The foregoing description of the Hospira license agreement is a summary only and is qualified in all respects by reference to the full text of that license agreement.

CJ Corp.

CJ markets Hextend in South Korea under an exclusive license from us. CJ paid us a license fee to acquire their right to market Hextend. CJ also pays us a royalty on sales of Hextend. 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. CJ is also responsible for obtaining the regulatory approvals required to manufacture and market PentaLyte, including conducting any clinical trials that may be required, and will bear all related costs and expenses.

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

Summit

We have entered into agreements with Summit to develop Hextend and PentaLyte in Japan, the People's Republic of China, and Taiwan. Summit has sublicensed to Maruishi the right to manufacture and market Hextend in Japan, and the right to manufacture and market Hextend and PentaLyte in China and Taiwan. The licenses do not include Hypothermic Use.

Table of Contents

Under the sublicense, Maruishi will complete clinical trials required and obtain regulatory approval to market the licensed products. Summit will also participate in the clinical trial and regulatory approval process. A Phase II clinical trial using Hextend in surgery is presently being conducted in Japan, and if the results are favorable, Summit plans to begin a Phase III trial during 2008. Maruishi will not be obligated to begin to seek regulatory approval of Hextend or PentaLyte in China and Taiwan earlier than six months after the results of the Phase II study of Hextend in Japan or our Phase II study of PentaLyte in the United States are made available to them, or March 2009, whichever is later.

The revenues from licensing fees, royalties, and net sales, and any other payments made for co-development, manufacturing, or marking rights to Hextend and PentaLyte in Japan will be shared between BioTime and Summit as follows: 40% to us and 60% to Summit. Net sales means the gross revenues from the sale of a product, less rebates, discounts, returns, transportation costs, sales taxes and import/export duties.

Summit paid us fees for the right to co-develop Hextend and PentaLyte in Japan, and Summit has also paid us a share of a sublicense fee payment from Maruishi. Additional milestone payments of 100,000,000 yen each, of which BioTime will receive 40%, are payable by Maruishi to Summit when a new drug application for Hextend is filed in Japan and when the new drug application is approved. The filing of a new drug application in Japan will not be done until clinical trials are completed, which could take several years. We will also be entitled to receive 40% of the royalties paid by Maruishi to Summit on sales in Japan. Royalties will range from 12% to 20% of net sales, depending upon the amount of Hext