SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended June 30, 2001

OR

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

For the transition period from _____ to _____

Commission File Number 0-22025

AASTROM BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Michigan	**94-3096597**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

24 Frank Lloyd Wright Drive
P. O. Box 376
Ann Arbor, MI 48106
(Address of principal executive offices, including zip code)
Registrant's telephone number, including area code: (734) 930-5555

Securities registered pursuant to Section 12(b) of the Act:
None
Securities registered pursuant to Section 12(g) of the Act:
Common Stock, no par value

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

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

The approximate aggregate market value of the registrant's Common Stock, no par value ("Common Stock"), held by non-affiliates of the registrant (based on the closing sales price of the Common Stock as reported on the Nasdaq National Market) on July 23, 2001 was approximately $100 million. Excludes shares of Common Stock held by directors, officers and each person who holds 5% or more of the outstanding shares of Common Stock, since such persons may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of September 10, 2001, 42,343,351 shares of Common Stock, no par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Document	**Form 10-K Reference**
Proxy Statement for the Annual Meeting of Shareholders scheduled for November 14, 2001	Items 10, 11, 12 and 13 of Part III

AASTROM BIOSCIENCES, INC.

ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

Except for the historical information presented, the matters discussed in this Report, including our product development and commercialization goals and expectations, potential market opportunities, our plans and anticipated results of our clinical development activities and the potential advantage of our products and product candidates under development, include forward-looking statements that involve risks and uncertainties. Our actual results may differ significantly from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed under the caption "Business Risks" in "Management's Discussion and Analysis of Financial Condition and Results of Operations." Unless the context requires otherwise, references to "we," "us," "our" and "Aastrom" refer to Aastrom Biosciences, Inc.

PART I

ITEM 1. BUSINESS

Aastrom Biosciences, Inc. is a leader in the development of human cell therapy products intended for a broad range of medical applications based on its patented process and device capabilities. Our lead cell therapeutic products under development include Dendricell™ products (DC-I and DCV-I) for the clinical-scale production of dendritic cells intended for the emerging cancer vaccine market. We are also developing our SC-I, CB-I and CB-II cell products for use in stem cell therapy and our OC-I cell product for the restoration of bone tissue.

Dendritic cells, a type of blood cell that have the ability to stimulate an immune response against specific targets, are being investigated as a potential new treatment for cancer and viral diseases. We intend to sell the DC-I cell product to clinical researchers and centers that are developing dendritic cell-based vaccines designed to treat cancer and other disorders. During the year ended June 30, 2001, we initiated our external site testing of the AastromReplicell™ System and the DC-I cell product with leading research centers. We intend to apply for CE Mark approval necessary for European marketing. We also plan to market the DC-I cell product to U.S. clinical and research groups that are developing dendritic cell-based cancer vaccines and to develop our own proprietary vaccines pending additional funding or strategic partnerships. Our stem cell therapy products have received CE Mark approval allowing us to begin commercialization activities in Europe, and are in Phase III-Type clinical studies in the U.S. Additionally, we have recently initiated a development program for the production of bone-forming cells in the AastromReplicell™ System. Our OC-I cell product is being developed for the treatment of patients with degenerative bone diseases such as osteoporosis and a Phase I/II-Pilot clinical study is in process in the U.S.

Our business model builds on two complementary components: (i) proprietary procedures and devices to enable certain types of stem cells and other types of human cells to be produced with excellent biological capabilities as compared with standard cell culture approaches, and (ii) the AastromReplicell™ System clinical platform that is designed to standardize and enable an effective commercialization pathway for bringing therapeutic cell production to medical practice. The AastromReplicell™ System consists of an instrumentation platform, to be integrated within the hospital or other centralized facility, that can operate a variety of single-use therapy kits that are specific to the desired medical application. Through this product configuration, we intend to either directly provide cells for therapeutic use, or enable customers or potential collaborators with the capability to produce cells for therapeutic applications through sale of the AastromReplicell™ System product line and cell therapy products. This approach is intended to provide a product pathway for each cell therapy that is similar to a pharmaceutical product including regulatory approval, reimbursement, marketing and pricing. We believe that the product design of the AastromReplicell™ System will allow us to develop additional cell therapy products to provide standardization for a number of emerging cell therapies being developed by other researchers.

Although we may not market the AastromReplicell™ System in the United States for stem cell therapy unless and until approval is obtained from the U.S. Food and Drug Administration (FDA), we have completed production-level versions of the AastromReplicell™ System and we have begun European commercialization activities for the AastromReplicell™ System instrumentation and the SC-I and CB-I therapy products. We may also market the AastromReplicell™ System in the U.S. for research and investigational use and we are developing our marketing plan to establish relationships with leading sites to build a customer foundation for the AastromReplicell™ System.

Cell Therapy

Cell therapy is the use of living cells in the treatment of medical disorders. These cells can either be used in conjunction with, or as a replacement to, traditional therapies. Cell therapy began with simple, but very effective, blood and platelet transfusions, and more recently has expanded to include specialized procedures including bone marrow, or stem cell transplants. In this procedure, stem cells are transplanted into patients to restore blood and immune system function that is damaged or destroyed by aggressive chemotherapy used to treat the cancer. Most recently, researchers are developing emerging cell therapies utilizing T-cells and dendritic cells to stimulate an immune response in patients with various forms of cancers, infectious diseases or viral infections. While these forms of cell therapy are emerging as potential new treatment options for several diseases, the success of cellular therapy is based, in part, on the need for care providers to be able to access therapeutic quantities of biologically active cells necessary for patient treatment. The AastromReplicell™ System is being developed to fill this need.

Cellular Immunotherapies

Cellular immunotherapy involves using cells of the immune system to eradicate a disease target. A number of research institutions and other companies are investigating T-lymphocytes (T-cells) and dendritic cells for this purpose. We anticipate that many of these procedures will require *ex vivo* cell production and manipulation, and present a significant market opportunity for our products and technologies.

Dendritic cells are blood system-derived cells that are believed to play an important role in the function of the immune system by presenting antigen to the immune system to trigger an immune response. Dendritic cells, when exposed to cancer cells or other pathogens, can serve as "educator" cells to activate other cells of the immune system. Researchers believe that cultured dendritic cells could augment the natural ability of a patient to present tumor antigens or antigens from infectious agents to the immune system and aid in the generation of a cytotoxic T-cell response to the offending agent.

In a study published in March 2000, researchers at leading German medical centers reported positive results of a new dendritic cell-based therapy. In this study, renal cell carcinoma patients were treated with dendritic cells that had been produced outside of the body, and then fused with tumor cells collected from the patient. The modified dendritic cells, once injected into the patient, triggered an immune response against the cancer in some patients. The results indicated a major new treatment modality against renal cell cancer. Further, additional clinical trials are currently underway at leading cancer centers to demonstrate the effectiveness of this new therapeutic approach in multiple cancer types. Common to these new therapeutic approaches is the requirement to culture and activate the dendritic cells outside of the patient (*ex vivo*). In these initial trials, production of the dendritic cells is performed using manual research laboratory equipment, open culture processes and specialized personnel. In order for these procedures to receive regulatory approval and to be used in standard medical practice, we believe that they must be standardized and implemented through user-friendly, sterilely-closed, automated and process-controlled products. The AastromReplicell™ System is designed to address this key need by enabling automated therapeutic dendritic cell production through a standardized product format.

T-cells, a class of lymphocyte white blood cells, play an important role in the human immune system and are responsible for the human immune response in a broad spectrum of diseases, including cancers and infectious diseases. Therapeutic procedures using Cytotoxic T-lymphocytes (CTLs) involve collecting T-cells from a patient and culturing them in an environment resulting in significantly increased numbers of T-cells with specificity for a particular disease target. Other companies and institutions have initiated clinical trials to demonstrate CTL effectiveness. The *ex vivo* production of these cells under conditions for use in medical treatment represents a critical step in the advancement of this therapy and the AastromReplicell™ System in being developed for this purpose.

We are developing our Dendricell™ products to provide a base dendritic cell for certain of these emerging immunotherapies. Following CE Mark approval, we intend to sell the Dendricell™ products to clinical researchers in Europe. In the U.S., we intend to sell the Dendricell™ for clinical research use, and we are evaluating plans to develop our own proprietary cancer vaccines using these products.

Stem Cell Therapy

Stem cell therapy is used for cancer patients who undergo chemotherapy or radiation therapy at dose levels that are toxic to the hematopoietic system, which is comprised of the bone marrow and the cells of the blood and immune system. In order to treat many cancers, high intensity chemotherapy or radiation therapy is often required, which may substantially destroy (myeloablate) or partially destroy (myelosuppress) the patient's hematopoietic system. The objective of stem cell therapy is to restore the patient's blood and immune system via the infusion and subsequent engraftment of healthy cells to replace the damaged bone marrow and result in the rapid recovery of neutrophils and platelets that have been destroyed by chemotherapy and radiation therapy. Stem cell therapy reduces the risk of life-threatening infections and bleeding episodes following cancer treatments.

Cells required for effective stem cell therapy include stem cells, to replenish depleted bone marrow and provide a long-term ongoing source of cells that make up the blood and immune system, and early and late stage hematopoietic progenitor cells, to provide for rapid neutrophil and platelet recoveries. Stromal accessory cells are believed to further augment the growth of bone marrow. In an adult, all of these cell types originate in the bone marrow. For traditional stem cell transplant procedures, these cells are currently collected from the donor or patient directly through multiple syringe aspirations under general anesthesia, known as bone marrow collection, or through blood apheresis following treatment with drugs which cause these cells to be released or mobilized from the bone marrow into the blood. This latter technique is known as a peripheral blood stem cell (PBSC) collection.

Once collected, the stem cell mixture is infused intravenously and the stem and stromal accessory cells migrate into the bone cavity where they engraft to form new marrow tissue. The hematopoietic progenitor cell components of the cell mixture provide early restoration of circulating white blood cells and platelets. The replenished bone marrow will normally provide long-term hematopoietic function, but complete restoration of bone marrow may, in some cases, take years following myeloablative cancer therapy. When the patient's hematopoietic system contains malignant cells, such as in the case of leukemia, stem cells from a suitable donor are generally required in order to avoid reintroducing the disease during cell infusion if stem cells for the transplant had been collected from the patient. Such donor-derived transplants are termed "allogeneic" transplants. Procedures using cells derived from the patient are termed "autologous" transplants.

The SC-I cell mixture is comprised of expanded bone marrow, including both hematopoietic and mesenchymal stem cells, and is intended for the restoration of normal blood and immune system function in patients that have undergone aggressive chemotherapy or radiation treatment. The SC-I cell mixture is intended to provide either an alternative method of obtaining cells used in stem cell transplantation, or to augment cells obtained through a PBSC collection in situations where it is difficult to obtain the desired quantity of PBSCs. We currently have a clinical trial evaluating the SC-I cell mixture in breast cancer patients and lymphoma patients. In this study, the SC-I cell mixture is being used to augment low-doses of PBSC that were collected from the patient.

Umbilical Cord Blood (CB), which is collected directly from the detached umbilical cord and placenta of newborn infants without pain or risk to the infant or the mother, is emerging as a new source of cells for stem cell therapy. This source of cells is being explored by physicians as a significant new development in stem cell therapy, but is currently limited by difficulties in obtaining sufficient quantities of these cells and by prolonged engraftment times for the cells once transplanted into the patient. See "Current Stem Cell Collection Methods." After collection, CB is typically frozen for later use in a stem cell therapy procedure. Storage of CB samples involves small volumes of cells, compared to typical bone marrow or PBSC storage. Accordingly, the costs of collection and storage of CB cells are comparatively low. CB may provide a tumor-free source of cells, making it a preferred source of cells for many current stem cell therapy procedures in cancer patients with metastatic disease (e.g. disease that has spread throughout the patient's body, affecting their own bone marrow and stem cells), and particularly in the absence of a suitably matched donor. Before CB can become a major supply source for stem cell therapy, a coordinated CB banking system

must emerge. In this regard, several CB banking programs have been established to date and are growing in both number and size. The establishment of these CB banking institutions is an initial step which may lead to a coordinated CB banking system.

As CB cells become available through coordinated banking efforts, we believe that the need for expansion becomes greater in order to provide larger quantities of cells for use in adult-sized patients. Our CB-I cell product is a mixture of stem and progenitor cells, produced from cord blood, that is intended to provide normal blood and immune system in leukemia patients following chemotherapy or radiation treatment. We currently have in process a clinical trial evaluating the CB-I cell product in adult leukemia patients.

Stem Cell Therapy Market Opportunity

Stem cell therapy is a widely used medical procedure in the treatment of patients with certain types of cancer. Industry sources estimate that up to 30,000 stem cell transplant procedures were performed annually. The estimated number of procedures has decreased as a result of a recent change in medical practice reducing the number of breast cancer patients receiving this treatment. Stem cell therapy, in the form of bone marrow transplantation, was originally used in patients who had received treatment for blood and bone marrow cancers such as leukemia, and genetic diseases of the blood. However, because stem cell therapy has been shown to promote the rapid recovery of hematopoietic function, it is now being used to enable patients with other forms of cancer to receive high dose or multicycle chemotherapy and radiation treatments. These high-intensity therapies are believed to have a greater probability of eradicating certain dose-sensitive cancers but, because of their hematopoietic toxicity, cannot generally be given without stem cell therapy. As a result, because of the current limitations of stem cell therapy some patients are treated with lower and less effective doses and fewer cycles of chemotherapy and radiation treatments than might otherwise be desired.

Stem cell therapy may also enhance the effectiveness of blood cell growth factors used. The timing and extent of additional cycles of chemotherapy is often limited by the recovery of a patient's white blood cells and platelets because a delayed recovery of these cells can leave the patient susceptible to life-threatening infection and bleeding episodes. This limitation may allow for the growth of residual tumor cells. Many cancer patients are routinely treated with growth factors including G-CSF, such as Neupogen, and GM-CSF, such as Leukine which enhance the development of mature circulating white blood cells and platelets from the early progenitor bone-marrow derived cells, thereby decreasing the time between cycles of therapy and the probability of infection. However, during high dose or multicycle therapy, the stem and progenitor cells on which these growth factors act are often depleted. Without these cells, growth factors have a limited or negligible affect. Stem cell therapy generally enhances the effectiveness of growth factors by introducing target stem and progenitor cells for growth factors to act upon such that patients generally exhibit a more rapid and consistent hematopoietic recovery.

Current Stem Cell Collection Methods

Currently, the bone marrow-derived cells required for stem cell therapy are collected primarily either through a bone marrow harvest or the PBSC collection method. Another source of stem cells is the blood that can be collected from the umbilical cord and placenta that is otherwise discarded following the birth of a child.

Bone Marrow Harvest

A traditional bone marrow harvest is a costly and invasive surgical procedure in which a physician removes approximately one liter of bone marrow from a patient or donor. This volume of bone marrow is removed using needles inserted into the cavity of the hip bone. The bone marrow harvest procedure typically requires between two to four hours of operating room time, with the physician often making more than 90 separate puncture sites in the hip bone to collect the necessary amount of bone marrow. Due to the length of the procedure and the trauma to the patient, general surgical anesthesia is administered and the patient is often hospitalized for one day. Frequently, the patient suffers pain from the procedure for several days after being discharged from the hospital. Furthermore, complications resulting from the general anesthesia or invasive nature of the procedure occur in a small percentage of patients. However, bone marrow harvest provides a reliable source of stem and stromal accessory cells.

PBSC Mobilization and Collection

PBSC mobilization is a technique in which bone marrow-derived cells are harvested from a patient's or donor's circulating blood, rather than from bone marrow. In a PBSC mobilization procedure, the patient or donor receives multiple injections of growth factors or cytotoxic drugs, or both, over the course of a week or more, which cause stem and progenitor cells resident in the bone marrow to mobilize into the circulating blood. The mobilized cells are then collected by connecting the patient or donor to a blood apheresis device, often times through the placement of a catheter, which draws and returns large volumes of the patient's or donor's blood in order to selectively remove the desired stem and progenitor cells. Each collection procedure typically lasts for two to six hours and is typically repeated on two to five consecutive days; however, procedure time has decreased and is expected to continue to decrease as the procedure is further optimized. Specialized laboratory testing over the period of mobilization and cell harvesting is necessary to determine that a sufficient quantity of desired cells has been collected, adding to the cost of the procedure. The PBSC process has become the predominant procedure in autologous stem cell therapy. However, for some patients, it is difficult to collect the desired, or an acceptable, quantity of PBSC for transplantation.

Procedure Considerations

Although stem cell therapy is being utilized to treat patients with a broader range of diseases, its availability continues to be limited by the high costs of procuring cells, the invasive nature of traditional cell procurement techniques, and by the technical difficulties related to those collection procedures. We believe that current charges for typical stem cell collection procedures through bone marrow harvest or PBSC collection range from $10,000 to $20,000 with considerable variability between institutions.

Overall costs of stem cell therapy include the costs of the cell collection and infusion procedures, and the costs associated with supporting the patient during post-transplant recovery. Post-transplant costs include hospitalization time, antibiotic support, management of adverse reactions, and infusions of platelets and red blood cells. Any new stem cell therapy process will generally need to provide similar recovery endpoints to be competitive with the current procedures. In this regard, PBSC procedures have gained popularity compared with bone marrow harvests because the number of platelet transfusions is reduced for some patients.

While CB is a promising new source of cells for transplantation, certain disadvantages exist including the relatively low number of available cells which may contribute to prolonged engraftment times for the cells once transplanted into the patient. Unlike bone marrow or PBSC harvest, where the collection of more cells to meet a particular treatment is typically achievable, the number of cells available from a CB donor is limited to the small quantity of cells available at the initial collection. This problem is exacerbated by the required cryopreservation of the cells, which causes additional cell loss. The resulting low cell number is believed to be responsible for the longer hematopoietic recovery times observed with CB transplants, as compared with bone marrow or PBSC transplants. Further, because of the low cell number, CB transplants are typically restricted to small patients. Therefore, increasing the number of therapeutic cells from a CB sample may facilitate the more widespread use of CB transplants. We believe that providing the transplant site with the capability to carry out the CB cell expansion will be a major factor in the increased use of CB for stem cell therapy and a significant business opportunity for us.

Products to implement a cell isolation method known as CD34 selection have been developed by other companies in conjunction with bone marrow harvest and PBSC collections. CD34 selection is a process designed to isolate specific types of cells in order to decrease storage and infusion problems associated with the large volume of fluids collected in bone marrow or multiple apheresis procedures and to assist in depleting T-cells and tumor cells from the transplant cells collected. CD34 selection is used after the initial collection of stem and progenitor cells and, therefore, can increase the difficulties or costs associated with the cell collection procedure.

Solid Tissue Cell Therapies

Bone marrow stromal cells (sometimes referred to as mesenchymal cells) may also contribute to the repair of degenerative bone diseases such as osteoporosis. Industry sources estimate that over 10 million Americans suffer from osteoporosis, a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially of the hip, spine and wrist. We have initiated a Phase I/II clinical study of our OC-I cell mixture to treat osteoporosis. The trial, will evaluate the AastromReplicell™ System to produce bone progenitor cells from a small amount of the patients own stem cells. The new expanded cells will then be infused intravenously with the intention to help restore the degenerated bone tissue. Trial results will focus on establishing safety and measuring bone formation, blood alkaline phosphatase and osteocalcin levels and bone catabolism.

Bone-forming cells may also have utility in certain localized procedures such as spinal fusion, hip and new implants and repair of large bone fractures. Currently, these medical procedures use artificial implants, either alone or with bone tissue from the patient (“autograft”). The autograft procedure is invasive, costly and generates substantial residual pain and discomfort for the patient. Our bone-forming cells may represent an alternative to these autograft procedures, and we are exploring this business direction.

A new form of cell therapy involves the production of chondrocytes for the restoration of cartilage. Chondrocyte therapy involves the surgical removal of a small amount of tissue from the patients knee and a production of therapeutic quantity of chondrocytes from this surgical biopsy. The cells are then implanted into the patients knee. Published reports indicate that such cells then reestablish mature articular cartilage. Currently, this cell production process is completed in highly specialized laboratory facilities using trained scientists and manual laboratory procedures. We believe that the AastromReplicell™ System may have the potential to reduce costs associated with the cell production procedure and, if successfully developed by us for this application, may eventually facilitate the transfer of the cell production capability away from specialized facilities directly to clinical care sites.

Aastrom Technology

Our technology platform consists of two components: (i) proprietary procedures and devices to enable certain types of stem cells and other types of human cells to be produced with superior biological capabilities as compared with standard cell culture approaches, and (ii) the AastromReplicell™ System clinical platform that is designed to standardize and enable an effective GMP-compliant commercialization pathway for bringing therapeutic cell production to medical practice. The AastromReplicell™ System consists of an instrumentation platform, to be integrated within the hospital or other centralized facilities, that can operate a variety of single-use therapy kits that are specific to the desired medical application. Through this product configuration, we intend to either directly provide cells for therapeutic use, or enable customers or potential collaborators with the capability to produce cells for therapeutic applications through sale of the AastromReplicell™ System product line and cell therapy products. This approach is intended to provide a product pathway for each cell therapy that is similar to a pharmaceutical product including regulatory approval, reimbursement, marketing and pricing. We believe that the product design of the AastromReplicell™ System will allow us to develop additional cell therapy products to provide standardization for a number of emerging cell therapies being developed by other researchers.

We are developing proprietary product and process technologies that are pioneering the *ex vivo* production of human stem and other tissue-specific progenitor cells. Our lead product, the AastromReplicell™ System utilizes our process technology and is designed to enable the *ex vivo* production of human stem and progenitor cells as an alternative or improvement to, bone marrow harvest and PBSC mobilization methods and to enhance the clinical utility of CB cells. The initial application of the AastromReplicell™ System is the production of cells for stem cell therapy. However, once established for use in stem cell therapy, we plan to leverage the cell production capabilities of the AastromReplicell™ System across multiple cell therapy opportunities as they develop. As these emerging cell therapies are developed, we intend to develop and introduce new therapy kits through collaborative relationships with others directed toward the treatment of cancer, infectious diseases, auto-immune diseases and in the restoration of solid tissues.

Core Technologies

Human Cell Growth Process

We have developed proprietary processes and patented technologies for *ex vivo* production of therapeutic stem and progenitor cells as well as other key cells found in human bone marrow. This proprietary process is called “single-pass perfusion” and provides a cell culture environment that attempts to mimic the biology and physiology of natural bone marrow. This process enables the production of stem and early and late-stage progenitor cells needed for an effective bone marrow stem cell therapy procedure. When this process is applied to other cell types, the resulting cell product appears to have enhanced biologic function as compared to cells produced through standard static culture processes. In pre-clinical studies performed at Aastrom, T-cells produced using our proprietary processes appear to have a significantly higher replicative capability. Further dendritic cells produced using this process appear to have an enhanced ability to present antigen to the immune system. We believe that these benefits can improve the overall clinical effectiveness of these procedures.

Growth factors can be added to stimulate specific cell lineages to grow or to increase cell growth to meet a particular therapeutic objective. The stem cell growth process can best be completed with little or no additional stem cell selection or purification procedures. This stem cell replication process can also enable or augment the genetic modification of cells by providing the cell division step needed for new genes to integrate into the stem cell DNA. Other currently available cell culture methods tend to result in a loss of stem cells, either through death or through differentiation into mature cells. The same medium-exchange perfusion approach that enables stem cells to grow improves the biological features of other types of human cells, compared with cells grown using standard cell culture techniques. We have exclusive rights to several issued U.S. patents that cover these processes and cell compositions. See “Additional Stem Cell and Other Cell Therapies.”

Aastrom Cell Culture Chamber

We have developed a proprietary cell culture chamber to implement our process technology. The culture chamber can produce cells on a clinical scale and allows for recovery of the cells for therapeutic use. Our pre-clinical data indicate that our cell culture chamber may be used for growing various types of human therapeutic cells, such as stem cells, T-cells and dendritic cells used for immunotherapies, chondrocytes for cartilage replacement, and mesenchymal tissues for bone and cartilage replacement. We hold exclusive rights to issued U.S. patents and additional applications for our cell culture chamber device technology. See “Additional Stem Cell and Other Cell Therapies.”

The AastromReplicell™ System

The AastromReplicell™ System is our proprietary clinical-scale cell production platform under development to enable the large scale *ex vivo* production of a variety of therapeutic cells at healthcare facilities, independent laboratories, transplant centers and blood banks, and has been designed to implement our stem

cell growth process as well as processes for the production of other cell types. The AastromReplicell™ System is comprised of several components, including single-use therapy kits such as the SC-I, CB-I, CB-II, OC-I and DC-I Therapy Kits, and microprocessor-controlled instruments. The single use therapy kits contain a Cell Cassette cartridge which contains our proprietary cell culture chamber, supply and waste reservoirs and harvest bag and process specific software which provides the cell production processing parameters to the AastromReplicell™ System instruments. The microprocessor-controlled instruments include the AastromReplicell™ System Incubator which controls the culture conditions for the operation of the AastromReplicell™ System Cell Cassette, and the Processor which automates the procedure sequences such as the inoculation of cells into, and harvesting of the cells from, the AastromReplicell™ System Cell Cassette. The AastromReplicell™ System Manager is a user interface computer that is being developed to simultaneously track and monitor the cell production process in multiple AastromReplicell™ System Incubators and record relevant process variables and operator actions.

The AastromReplicell™ System is designed to be operated with minimal operator activity by a medical or laboratory technician and can implement clinical scale cell production at the patient care site. The end product of the AastromReplicell™ System process is a blood-bag container with the cell product. The control and documentation features of the AastromReplicell™ System have been designed to meet good manufacturing practice (GMP) requirements for the therapeutic production of cells. The product configuration of the AastromReplicell™ System consists of an instrumentation platform, to be integrated within the hospital or other centralized facility, that can operate a variety of single-use therapy kits that are specific to the desired medical application. This is intended to provide a product pathway for each cell therapy that is similar to a pharmaceutical product including regulatory approval, reimbursement, marketing and pricing. We believe that the product design of the AastromReplicell™ System will allow us to develop additional cell therapy kits to provide a commercialization pathway for a number of emerging cell therapies being developed by other researchers.

Efficient Gene Transfer

We have developed proprietary processes and device technology that may enable increased efficiency of vector-mediated *ex vivo* gene transfer into cells as compared to conventional procedures. This directed-motion gene transfer or gene loading technology has potential application in most cell and tissue types and most vector technologies. Subject to the availability of funding, we intend to develop products based upon our gene loading technology. Development of additional products, however, will require us to raise additional funds or to seek collaborative partners, or both, to finance related research and development activities, as to which there can be no assurance of success. Furthermore, due to the uncertainties involved, we are unable to estimate the length of time such development may take. If successfully developed into products, we believe that such products could facilitate the advancement of numerous gene therapy protocols into the clinic and ultimately the market. We have exclusive rights to issued U.S. patents, and have additional applications pending, for this technology. See "Aastrom Product Candidates For *Ex Vivo* Gene Therapy."

AastromReplicell™ System for Stem Cell Therapy

Our initial application for the AastromReplicell™ System is in the field of stem cell therapy, where we believe that the AastromReplicell™ System addresses certain of the limitations of existing procedures. The AastromReplicell™ System is based on a comparatively simple process in which a small volume of bone marrow cells are collected from the patient or donor using a needle aspiration procedure, typically under a local anesthetic or sedative. Alternatively, CB cells have been shown to be a new source of cells for use in stem cell transplantation. The starting mixture of either bone marrow or CB cells is quantified, and an appropriate volume of cells is then inoculated into one or more AastromReplicell™ System Cell Cassettes with the necessary growth media. Using the AastromReplicell™ System, growth-factor-stimulated cells are produced in approximately 12 days with no further patient involvement. Depending upon the cell quantity necessary for a therapeutic application, single or multiple AastromReplicell™ System Cell Cassettes may be required, with a different volume requirement of starting cells taken from the patient at the initial visit or obtained from the CB bank. The AastromReplicell™ System has been designed to minimize operator involvement during the cell production process, and the steps required before and after the AastromReplicell™ System are standard laboratory procedures. Cells derived from CB may also serve as a tumor-free source of stem and progenitor cells for expansion in the AastromReplicell™ System.

Potential Advantages of AastromReplicell™ System

The AastromReplicell™ System is designed to enable a cost-efficient and minimally invasive alternative, or supplement, to existing procedures, which could offer numerous advantages for both patients and medical staff:

The AastromReplicell™ System can generate larger quantities of cells from a small starting sample. Alternative procedures to obtain the large quantity of stem cells necessary for transplantation require a patient to endure up to approximately 40 hours of procedure time or up to approximately 100 invasive needle sticks to obtain the necessary quantity of stem cells required for the transplant. The AastromReplicell™ System offers an alternative that requires less than two hours of procedure time and significantly fewer needle sticks.

The AastromReplicell™ System enables the production of certain cells, such as umbilical cord blood (CB) cells, for which there might otherwise be insufficient quantities available for many transplants. Having access to a sufficient number of cells is essential to successful clinical outcomes. This is particularly the case with umbilical cord blood transplants. This source of stem cells is increasingly being used as an alternative to traditional stem cell transplant procedures. However, the limited quantities of available cells and difficulties in expanding the starting volumes to therapeutic quantities have restricted the widespread practice of CB transplants. The AastromReplicell™ System is designed to solve this dilemma by providing the capability to easily and cost-effectively expand CB cells to higher quantities for therapeutic treatments.

Pre-clinical tests have demonstrated tumor cell purging of certain cancer cells in the AastromReplicell™ System expansion process. Cancer patients with tumor metastases, in which the cancer has spread to the blood and bone marrow, have not traditionally been candidates for autologous stem cell transplants because such transplant might reintroduce cancer cells into the patient. Additionally, patients may have undetected tumor cells present in their marrow or PBSC transplant, which could re-establish cancer in the patient following transplant. Our initial pre-clinical results, as well as studies conducted by third-party investigators, have shown that some primary human tumor cells die or do not grow during hematopoietic cell culture. The smaller volume of starting cells used for the AastromReplicell™ System compared with bone marrow harvest or PBSC transplants may provide approximately 10 to 70 fold less tumor cells in a transplant. Further, in an evaluation of 14 tumor-contaminated bone marrow samples that were expanded with the AastromReplicell™ System process, the presence of breast cancer cells in each sample was either substantially reduced or was no longer detectable. Tumor cells that were detectable after expansion in the AastromReplicell™ System showed a significant reduction in clonogenicity (the ability to replicate). We believe that this combination of passive depletion during culture with the lower starting volume of tumor cells may result in a tumor-free or tumor-reduced cell product for transplant. The clinical benefit of such tumor depletion, if any, will vary depending upon the type of cancer and state of disease.

Supplemental therapy with AastromReplicell™ System produced cells. Collection of cells for transplant is a variable procedure requiring longer collection procedures for some patients compared to others. The AastromReplicell™ System offers a means to augment current collection techniques, thereby reducing variability and the overall collection burden for the patient and care provider.

The AastromReplicell™ System automates the process of growing human cells and is designed to be used directly in a hospital setting. Growing human cells has largely been a research laboratory process, requiring substantial time and technical expertise. The AastromReplicell™ System is designed to provide sterilely-closed, automated cell production capabilities directly at the patient care site in compliance with regulatory standards, providing process reliability and reducing the need for highly skilled operators.

Clinical Development

The AastromReplicell™ System is an automated clinical system designed to be used by medical personnel at hospitals and patient care centers to produce therapeutic cells for the treatment of a broad range of diseases, including cancer, infectious diseases and the restoration of solid tissues.

The AastromReplicell™ System is designed as a family of products consisting of an instrumentation platform that operates single-use, patient-specific, therapy kits. Each therapy kit, which is specific to the desired cell or tissue type, is operated by the AastromReplicell™ System instrument platform, which automates the otherwise complex cell production processes. This instrument platform allows for on-site cell manufacturing directly at the hospital, that is compliant with GMPs. The process instructions contained within each therapy kit, and where applicable, the reagents, growth medium and cytokines, are specific for the production of each cell type. This product design feature provides for a variety of therapy kits to be integrated into the AastromReplicell™ System product line.

The AastromReplicell™ System is being evaluated in multi-site clinical trials in the U.S. under Investigational Device Exemptions (IDEs) from the FDA. The initial goals of our clinical trial program are to obtain a Pre-Market Approval (PMA) in the U.S., necessary to market the AastromReplicell™ System for autologous stem cell therapy and umbilical cord blood transplants, and to support European marketing activities.

We have conducted clinical trials in the U.S. evaluating stem cells produced in the AastromReplicell™ System from a small starting amount of bone marrow. Results from initial studies demonstrated the ability of the AastromReplicell™ System to safely and reliably produce stem and progenitor cells that engraft and restore blood and immune system function in cancer patients who had undergone very aggressive chemotherapy. Further, the small volume aspirate, along with a purging of contaminated tumor cells during the stem cell production has indicated a way to offer patients a transplant with a lower risk of receiving back tumor cells.

We are now conducting a randomized U.S. clinical trial evaluating the AastromReplicell™ System to compliment traditional therapies by augmenting stem cells collected from a single PBSC apheresis procedure. The objectives of this study are to demonstrate that an optimal targeted recovery can be achieved using the AastromReplicell™ System-produced cells with a sub-optimal PBSC cell dose that otherwise would not provide this desired outcome. This procedure appears to improve the certainty of procedure outcome by providing a more reliable means of cell collection and patient recovery.

We have also conducted clinical feasibility trials to evaluate CB cells produced in the AastromReplicell™ System to improve recoveries of pediatric and adult patients requiring donor derived (or allogeneic) stem cell transplants. Results of the pediatric transplants indicated that AastromReplicell™ System-produced cells were safe and well tolerated by the patients, and an improvement in 100-day post-transplant survival for the patients was observed. Results from our adult cord blood trial suggested that the AastromReplicell™ System could increase the quantity of cord blood cells available and enable adult-sized patients to undergo a transplant when they may not otherwise be CB transplant candidates due to low cell dose. We have extended these trials into a comparative trial with concurrent controls. Several CB banking institutions are now being established by other organizations. This banking infrastructure, together with the expansion capabilities of the AastromReplicell™ System, may lead to CB as a promising new source of cells for therapeutic use.

The preliminary results of our pre-pivotal trials may not be indicative of results that will be obtained from subsequent patients in the trials or from more extensive trials. Further, there can be no assurance that our pre-pivotal or pivotal trials will be successful, or that biologic license application (BLA) registration or required foreign regulatory approvals for the AastromReplicell™ System will be obtained in a timely fashion, or at all. See “Business Risks.”

Additional Stem Cell and Other Cell Therapies

Our development efforts have been focused on the development of the SC-I Therapy Kit for the production of bone marrow stem cells and the CB-I Therapy Kit for the production of cord blood cells. We believe that additional therapy kits may be developed for application to a variety of other emerging cell therapies in addition to hematopoietic stem cell therapy. The AastromReplicell™ System has the potential to supplant current manual cell culture methods to produce therapeutic quantities of cell types such as T-cells, dendritic cells, cell-based cancer vaccines, chondrocytes, mesenchymal cells, keratinocytes and neuronal cells. Other than a limited application of chondrocyte therapy, novel cell therapies are still in early stages of development by third parties, and no assurance can be given that such other cell therapies will be successfully developed. Potential advantages of the AastromReplicell™ System in these therapies may include: (i) reducing labor and capital costs; (ii) enhancing process reliability; (iii) automating quality assurance and process record keeping; (iv) reducing the need for specialized, environmentally controlled facilities; and (v) providing greater accessibility of these procedures to care providers and patients, and (vi) in certain cases, providing a more biologically active cell product.

Modification of such processes and application of our products to the expansion of other cell types will require additional development of specialized cell culture capabilities which may need to be incorporated within our existing product platform. Such modifications may require us to raise substantial additional funds, or to seek additional collaborative partners, or both. There can be no assurance that we will be able to successfully modify or develop existing or future products to enable such additional cell production processes. Our business opportunity is dependent upon successful development and regulatory approval of these novel cell therapies. No assurance can be given that such novel therapies will be successfully developed by other companies or approved by applicable regulatory authorities, or that our processes or product candidates will find successful application in such therapies. In addition, we may be required to obtain license rights to such technologies in order to develop or modify existing or future products for use in such therapies. No assurance can be given that we will be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. See “Clinical Development” and “Business Risks.”

Aastrom Product Candidates for *Ex Vivo* Gene Therapy

A novel form of cell therapy is *ex vivo* gene therapy. For this type of cell therapy, cells collected from the patient or a donor are genetically modified prior to their infusion into the patient. Similar to other cell therapies, the ability to produce a therapeutic dose of these gene-modified cells is a major limitation to the commercialization of these cell therapies. This limitation is further exacerbated by the additional requirement that the cells be genetically modified under conditions that are sterile and comply with GMP.

Gene therapy is a therapeutic modality that holds the potential to significantly impact the delivery of healthcare and the delivery of therapeutically useful protein-based drugs within the body. Gene therapies are generally targeted at the introduction of a missing normal gene into otherwise defective human tissue, or the introduction of novel biologic capability into the body via the introduction of a gene not ordinarily present. The major developmental focus of the *ex vivo* gene therapy industry has been to identify the therapeutic gene of interest, insert it into a suitable vector that can be used to transport and integrate the gene into the DNA of the target cell, and then cause the gene to become expressed. We believe that for *ex vivo* gene therapy to progress to clinical applications, a process to produce a sufficient quantity of therapeutic cells is required for many such therapies as is an efficient means to insert the gene vector into target cells. Gene therapy is still in an early stage of development by third parties. Our business opportunity is dependent upon the successful development and regulatory approval of individual gene therapy applications. No assurance can be given that such applications will be developed or approved or that our processes or product candidates will find successful applications in such therapies. Successful development of our processes and product candidates for application in *ex vivo* gene therapy will require substantial additional research and development, including clinical testing, and will be subject to our ability to finance such activities on acceptable terms, if at all. See “Business Risks.”

The AastromReplicell™ System for Gene Therapy

The AastromReplicell™ System has been designed to produce cells for therapy, and we believe that the AastromReplicell™ System may be useful in many potential *ex vivo* gene therapy applications. Further, we anticipate that our proprietary stem cell production process technology implemented by the AastromReplicell™ System may provide the conditions for clinical scale stem cell division, and enable or enhance the introduction of therapeutic genes into stem cell DNA. We believe that our technology may also enable expansion of more mature progeny of these stem cells to create a gene therapy cell product with potential short and long term therapeutic affect.

Our technologies are intended to provide two capabilities in *ex vivo* gene therapy: (i) the enablement of stem cell gene therapies for a variety of hematologic and other disorders, based on the AastromReplicell™ System's ability to enable large scale stem cell division *ex vivo;* and (ii) the enablement of gene transfer and therapeutic cell production by local and regional primary patient care facilities and ancillary service laboratories.

The Aastrom™ Gene Loader

The Aastrom™ Gene Loader process technology, which is under development, is designed to enhance the efficiency and reliability of the transfer of new therapeutic genes, which are carried by vectors, into the target cell. This process, which is typically inefficient in many human cells, may inhibit *ex vivo* gene therapies from moving forward in the clinic. The Aastrom™ Gene Loader incorporates our proprietary directed-motion gene transfer technology and is designed to overcome this limitation. Complete product development is expected to require additional funding sources or collaborations with others, or both.

We believe that these issues represent a general bottleneck for other companies pursuing clinical *ex vivo* gene therapy applications. Our technology under development may favorably influence these gene therapy applications, the development of which are impeded due to low transduction efficiencies and the resultant need for use of large quantities of gene vectors and/or target delivery tissues.

Manufacturing

We have established relationships with third party manufacturers which are FDA registered as suppliers for the manufacture of medical products to manufacture various components of the AastromReplicell™ System.

In April 1998, we entered into a manufacturing agreement with SeaMED for the commercial manufacturing of the instrument components of the AastromReplicell™ System. The initial term of the manufacturing agreement was until April 2001, after which the agreement is automatically renewed until terminated upon a 24-month notice from SeaMED or a 6-month notice from us. We retain all proprietary rights to our intellectual property which is utilized by SeaMED pursuant to this agreement.

In March 1996, we entered into a License and Supply Agreement with Immunex Corporation for an initial five-year term to purchase and resell certain cytokines and ancillary materials for use in conjunction with the AastromReplicell™ System. The agreement, as amended, allows for us to extend the term for successive two-year terms upon written notice, notice of which has been provided by us extending the agreement through March 2003 and is subject to certain minimum purchase requirements. The agreement provided for Immunex to receive up-front and renewal fees totaling $5,500,000. Pursuant to agreements between Immunex and Aastrom, the annual fees due in March 1998, 1999 and 2000 were each paid by us through the issuance of $1,100,000 in our common stock. In August 1997, Aastrom and Immunex amended the agreement to expand our territorial rights to use and sell such materials on a worldwide basis. The supply agreement may be terminated by either party effective immediately upon written notice of termination to the other party in the event that such party materially breaches the agreement and such breach continues unremedied after notice and expiration of a specified cure period or in the event that a bankruptcy proceeding is commenced against a party and is not dismissed or stayed within a 45-day period. In addition, Immunex has the right to cease the supply to us of cytokines and ancillary materials if we fail to purchase a minimum amount of our forecasted annual needs from Immunex after notice to us and expiration of a specified cure period. In the event that Immunex elects to cease to supply to us cytokines and ancillary materials or is prevented from supplying such materials to us by reason of force majeure, limited manufacturing rights will be transferred to us under certain circumstances. There is, however, no assurance that we could successfully manufacture the compounds ourselves or identify others that could manufacture these compounds to acceptable quality standards and costs, if at all.

In December 1996, we entered into a Collaborative Supply Agreement with Anchor Advanced Products, Inc., Mid-State Plastics Division (MSP), now a division company of Moll Industries. Under this agreement, MSP conducted both pre-production manufacturing development and now commercial manufacturing and assembly of the Cell Cassette component of the AastromReplicell™ System for us. Throughout the term of this agreement, we have agreed to treat MSP as our preferred supplier of Cell Cassettes, using MSP as our supplier of at least 60% of our requirements for Cell Cassettes.

There can be no assurance that we will be able to continue our present arrangements with our suppliers, supplement existing relationships or establish new relationships or that we will be able to identify and obtain the ancillary materials that are necessary to develop our product candidates in the future. Our dependence upon third parties for the supply and manufacture of such items could adversely affect our ability to develop and deliver commercially feasible products on a timely and competitive basis. See "Business Risks."

Patents and Proprietary Rights

Our success depends in part on our ability, and the ability of our licensors, to obtain patent protection for our products and processes. We have exclusive rights to over 20 issued U.S. patents, and non-exclusive rights to one other issued U.S. patent. These patents present claims to (i) certain methods for *ex vivo* stem cell division as well as *ex vivo* human hematopoietic stem cell stable genetic transformation and expanding and harvesting a human hematopoietic stem cell pool; (ii) certain apparatus for cell culturing, including a bioreactor suitable for culturing human stem cells or human hematopoietic cells; (iii) certain methods of infecting or transfecting target cells with vectors; and (iv) a cell composition containing human stem cells or progenitor cells, or genetically modified stem cells, when such cells are produced in an *ex vivo* medium exchange culture. Certain patent equivalents to the U.S. patents have also been issued in other jurisdictions including Australia, Canada and under the European Patent Convention. These patents are due to expire beginning in 2006. In addition, we and our exclusive licensors have filed applications for patents in the United States and equivalent applications in certain other countries claiming other aspects of our products and processes, including a number of U.S. patent applications and corresponding applications in other countries related to various components of the AastromReplicell™ System.

The validity and breadth of claims in medical technology patents involve complex legal and factual questions and, therefore, may be highly uncertain. No assurance can be given that any patents based on pending patent applications or any future patent applications of us, or our licensors, will be issued, that the scope of any patent protection will exclude competitors or provide competitive advantages to us, that any of the patents that have been or may be issued to us or our licensors will be held valid if subsequently challenged or that others will not claim rights in or ownership of the patents and other proprietary rights held or licensed by us. Furthermore, there can be no assurance that others have not developed or will not develop similar products, duplicate any of our products or design around any patents that have been or may be issued to us or our licensors. Since patent applications in the United States are maintained in secrecy until patents issue, we also cannot be certain that others did not first file applications for inventions covered by our, and our licensors' pending patent applications, nor can we be certain that we will not infringe any patents that may be issued to others on such applications.

We rely on certain licenses granted by the University of Michigan and others for certain patent rights. If we breach such agreements or otherwise fails to comply with such agreements, or if such agreements expire or are otherwise terminated, we may lose our rights in such patents, which would have a material

adverse affect on our business, financial condition and results of operations. See “Research and License Agreements.”

We also rely on trade secrets and unpatentable know-how that we seek to protect, in part, by confidentiality agreements. It is our policy to require our employees, consultants, contractors, manufacturers, outside scientific collaborators and sponsored researchers, and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual’s relationship with us is to be kept confidential and not disclosed to third parties except in specific limited circumstances. We also require signed confidentiality or material transfer agreements from any company that is to receive our confidential information. In the case of employees, consultants and contractors, the agreements generally provide that all inventions conceived by the individual while rendering services to us shall be assigned to us as the exclusive property of Aastrom. There can be no assurance, however, that these agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets or unpatentable know-how will not otherwise become known or be independently developed by competitors.

Our success will also depend in part on our ability to develop commercially viable products without infringing the proprietary rights of others. We have not conducted freedom of use patent searches and no assurance can be given that patents do not exist or could not be filed which would have an adverse affect on our ability to market our products or maintain our competitive position with respect to our products. If our technology components, devices, designs, products, processes or other subject matter are claimed under other existing United States or foreign patents or are otherwise protected by third party proprietary rights, we may be subject to infringement actions. In such event, we may challenge the validity of such patents or other proprietary rights or be required to obtain licenses from such companies in order to develop, manufacture or market our products. There can be no assurances that we would be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. Furthermore, the failure to either develop a commercially viable alternative or obtain such licenses could result in delays in marketing our proposed products or the inability to proceed with the development, manufacture or sale of products requiring such licenses, which could have a material adverse affect on our business, financial condition and results of operations. If we are required to defend ourself against charges of patent infringement or to protect our proprietary rights against third parties, substantial costs will be incurred regardless of whether we are successful. Such proceedings are typically protracted with no certainty of success. An adverse outcome could subject us to significant liabilities to third parties and force us to curtail or cease our development and sale of our products and processes.

Certain of our, and our licensors’, research has been or is being funded in part by the Department of Commerce and by a Small Business Innovation Research Grant obtained from the Department of Health and Human Services. As a result of such funding, the U.S. Government has certain rights in the technology developed with the funding. These rights include a non-exclusive, paid-up, worldwide license under such inventions for any governmental purpose. In addition, the government has the right to require us to grant an exclusive license under any of such inventions to a third party if the government determines that (i) adequate steps have not been taken to commercialize such inventions, (ii) such action is necessary to meet public health or safety needs or (iii) such action is necessary to meet requirements for public use under federal regulations. Additionally, under the federal Bayh Dole Act, a party which acquires an exclusive license for an invention that was partially funded by a federal research grant is subject to the following government rights: (i) products using the invention which are sold in the United States are to be manufactured substantially in the United States, unless a waiver is obtained; (ii) if the licensee does not pursue reasonable commercialization of a needed product using the invention, the government may force the granting of a license to a third party who will make and sell the needed product; and (iii) the U.S. Government may use the invention for its own needs.

Research and License Agreements

In March 1992, we entered into a License Agreement with the University of Michigan, as contemplated by a Research Agreement executed in August 1989 relating to the *ex vivo* production of human cells. Pursuant to this License Agreement, as amended (i) we acquired exclusive worldwide license rights to the patents and know-how for the production of blood cells and bone marrow cells as described in the University of Michigan’s research project or which resulted from certain further research conducted through December 1994, and (ii) we are obligated to pay to the University of Michigan a royalty equal to 2% of the net sales of products which are covered by the University of Michigan’s patents. Unless it is terminated earlier at our option or due to a material breach by us, the License Agreement will continue in affect until the latest expiration date of the patents to which the License Agreement applies.

Government Regulation

Our research and development activities and the manufacturing and marketing of our products are subject to the laws and regulations of governmental authorities in the United States and other countries in which our products will be marketed. Specifically, in the United States, the FDA, among other activities, regulates new product approvals to establish safety and efficacy of these products. Governments in other countries have similar requirements for testing and marketing. In the United States, in addition to meeting FDA regulations, we are also subject to other federal laws, such as the Occupational Safety and Health Act and the Environmental Protection Act, as well as certain state laws.

Regulatory Process in the United States

To our knowledge, we are the first to develop a GMP-compliant cell culture system for *ex vivo* human cell production to be sold for therapeutic applications. Therefore, to a certain degree, the manner in which the FDA will regulate our products is uncertain.

Our products are potentially subject to regulation as medical devices under the Federal Food, Drug and Cosmetic Act, and as biological products under the Public Health Service Act. Different regulatory requirements may apply to our products depending on how they are categorized by the FDA under these laws. The FDA has indicated that it intends to regulate the cells produced in the AastromReplicell™ System as licensed biologic through the Center for Biologics Evaluation and Research. However, there can be no assurance that FDA will ultimately regulate the AastromReplicell™ System in this manner.

The FDA is still in the process of developing its requirements with respect to somatic cell therapy and gene cell therapy products and has issued draft documents concerning the regulation of umbilical cord blood stem cell products, as well as cellular and tissue-based products. If the FDA adopts the regulatory approach set forth in the draft document, the FDA will require regulatory approval for certain human cellular or tissue based products, including cells produced in the AastromReplicell System, through a biologic license application (BLA).

The FDA has published regulations which require registration of certain facilities, which may include our customers, and is in the process of publishing regulations for the manufacture of human cellular or tissue based products (HC/TPs) which may impact our customers. We believe that the fixed validated process in a sterile disposable provided by our products will assist our customers in meeting these requirements, but the regulations may change prior to final release.

Approval of new medical devices and biological products is a lengthy procedure leading from development of a new product through preclinical and clinical testing. This process takes a number of years and the expenditure of significant resources. There can be no assurance that Aastroms product candidates will ultimately receive regulatory approval.

Regardless of how our product candidates are regulated, the Federal Food, Drug, and Cosmetic Act and other Federal statutes and regulations govern or influence the research, testing, manufacture, safety, labeling, storage, recordkeeping, approval, distribution, use, reporting, advertising and promotion of such products. Noncompliance with applicable requirements can result in civil penalties, recall, injunction or seizure of products, refusal of the government to approve

or clear product approval applications or to allow us to enter into government supply contracts, withdrawal of previously approved applications and criminal prosecution.

Product Approval

In order to obtain FDA approval of a new medical product, sponsors must generally submit proof of safety and efficacy. In some cases, such proof entails extensive preclinical and clinical laboratory tests. The testing, preparation of necessary applications and processing of those applications by the FDA is expensive and may take several years to complete. There can be no assurance that the FDA will act favorably or in a timely manner in reviewing submitted applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals which could delay or preclude us from marketing any products we may develop. The FDA may also require post-marketing testing and surveillance of approved products, or place other conditions on the approvals. These requirements could cause it to be more difficult or expensive to sell the products, and could therefore restrict the commercial applications of such products. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. For patented technologies, delays imposed by the governmental approval process may materially reduce the period during which we will have the exclusive right to exploit such technologies.

If human clinical trials of a proposed medical product are required, the manufacturer or distributor of the product will have to file an IDE or investigational new drug (IND) submission with the FDA prior to commencing human clinical trials. The submission must be supported by data, typically including the results of pre-clinical and laboratory testing. Following submission of the IDE or IND, the FDA has 30 days to review the application and raise safety and other clinical trial issues. If we are not notified of objections within that period, clinical trials may be initiated, and human clinical trials may commence at a specified number of investigational sites with the number of patients approved by the FDA. We have submitted several IDEs for the AastromReplicell™ System, and have conducted clinical studies under these IDEs.

Some of our products may be classified as Class II or Class III medical devices. The FDA categorizes devices into three regulatory classifications subject to varying degrees of regulatory control. In general, Class I devices require compliance with labeling and record keeping regulations, Quality System Regulation (QSR), 510(k) pre-market notification, and are subject to other general controls. Class II devices may be subject to additional regulatory controls, including performance standards and other special controls, such as post-market surveillance. Class III devices, which are either invasive or life-sustaining products, or new products never before marketed (for example, non-"substantially equivalent" devices), require clinical testing to demonstrate safety and effectiveness and FDA approval of a PMA prior to marketing and distribution. The FDA also has the authority to require clinical testing of Class I and Class II devices.

We, and any contract manufacturer, may be required to be registered as a medical device manufacturer with the FDA. As such, they will be inspected on a routine basis by the FDA for compliance with the FDAs QSR regulations. These regulations would require that we, and any contract manufacturer, design, manufacture and service products and maintain documents in a prescribed manner with respect to manufacturing, testing, distribution, storage, design control and service activities. The Medical Device Reporting regulation requires that we provide information to the FDA on deaths or serious injuries alleged to be associated with the use of our devices, as well as product malfunctions that are likely to cause or contribute to death or serious injury if the malfunction were to recur. In addition, the FDA prohibits a company from promoting an approved device for unapproved applications and reviews company labeling for accuracy.

We believe that the cells produced in the AastromReplicell™ System will be regulated by the FDA as a licensed biologic, although there can be no assurance that the FDA will not choose to regulate this product in a different manner. The FDA categorizes human cell or tissue based products as either minimally manipulated or more than minimally manipulated, and has propsed that more than minimally manipulated products be regulated through a "tiered approach intended to regulate human cellular and tissue based products only to the extent necessary to protect public health." For products which may be regulated as biologics, the FDA requires (i) preclinical laboratory and animal testing, (ii) submission to the FDA of an investigational new drug (IND) or investigational device exemption (IDE) application which must be effective prior to the initiation of human clinical studies, (iii) adequate and well-controlled clinical trials to establish the safety and efficacy of the product for its intended use, (iv) submission to the FDA of a biologic license application (BLA) and (v) review and approval of the BLA as well as inspections of the manufacturing facility by the FDA prior to commercial marketing of the product.

Preclinical testing covers laboratory evaluation of product chemistry and formulation as well as animal studies to assess the safety and efficacy of the product. The results of these tests are submitted to the FDA as part of the IND. Following the submission of an IND, the FDA has 30 days to review the application and raise safety and other clinical trial issues. If we are not notified of objections within that period, clinical trials may be initiated. Clinical trials are typically conducted in three sequential phases. Phase I represents the initial administration of the drug or biologic to a small group of humans, either healthy volunteers or patients, to test for safety and other relevant factors. Phase II involves studies in a small number of patients to assess the efficacy of the product, to ascertain dose tolerance and the optimal dose range and to gather additional data relating to safety and potential adverse affects. Once an investigational drug is found to have some efficacy and an acceptable safety profile in the targeted patient population, multi-center Phase III studies are initiated to establish safety and efficacy in an expanded patient population and multiple clinical study sites. The FDA reviews both the clinical plans and the results of the trials and may request us to discontinue the trials at any time if there are significant safety issues.

The results of the preclinical tests and clinical trials are submitted to the FDA in the form of a BLA for marketing approval. The testing and approval process is likely to require substantial time and effort and there can be no assurance that any approval will be granted on a timely basis, if at all. Additional animal studies or clinical trials may be requested during the FDA review period that may delay marketing approval. After FDA approval for the initial indications, further clinical trials may be necessary to gain approval for the use of the product for additional indications. The FDA requires that adverse affects be reported to the FDA and may also require post-marketing testing to monitor for adverse affects, which can involve significant expense.

Under current requirements, facilities manufacturing biological products must be licensed. To accomplish this, a BLA must be filed with the FDA. The BLA describes the facilities, equipment and personnel involved in the manufacturing process. An establishment license is granted on the basis of inspections of the applicants facilities in which the primary focus is on compliance with GMPs and the ability to consistently manufacture the product in the facility in accordance with the BLA. If the FDA finds the inspection unsatisfactory, it may decline to approve the BLA, resulting in a delay in production of products.

As part of the approval process for human biological products, each manufacturing facility must be registered and inspected by the FDA prior to marketing approval. In addition, state agency inspections and approvals may also be required for a biological product to be shipped out of state.

Regulatory Process in Europe

The AastromReplicell™ instruments and disposables are currently being regulated in Europe as a Class I Sterile or Class IIb medical device, under the authority of the new Medical Device Directives (MDD) being implemented by European Union (EU) member countries. These classifications apply to medical laboratory equipment and supplies including, among other products, many devices that are used for the collection and processing of blood for patient therapy. Certain ancillary products (e.g., biological reagents) used as part of the AastromReplicell™ System are treated as Class III medical devices.

The MDD regulations vest the authority to permit affixing of the CE Mark with various Notified Bodies. These are private and state organizations which operate under license from the member states of the EU to certify that appropriate quality assurance standards and compliance procedures are followed by developers and manufacturers of medical device products or, alternatively, that a manufactured medical product meets a more limited set of requirements. Notified Bodies are also given the responsibility for determination of the appropriate standards to apply to a medical product. Receipt of permission to affix the

CE Mark enables a company to sell a medical device in all EU member countries. Other registration requirements may also need to be satisfied in certain countries.

During 1999, we received permission from our Notified Body (The British Standards Institute) to affix the CE Mark to the AastromReplicell™ instrumentation and components for the SC-I Therapy Kit and CB-I Therapy Kit. This has allowed us to market these products in the European Union. There can be no assurance that the AastromReplicell™ System will continue to be regulated under its current status, any change in which would affect our ability to sell the product and adversely affect our business, financial condition and results of operations.

Competition

The biotechnology and medical device industries are characterized by rapidly evolving technology and intense competition. Our competitors include major pharmaceutical, medical device, medical products, chemical and specialized biotechnology companies, many of which have financial, technical and marketing resources significantly greater than ours. In addition, many biotechnology companies have formed collaborations with large, established companies to support research, development and commercialization of products that may be competitive with ours. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize products on their own or through joint ventures. Our product development efforts are primarily directed toward obtaining regulatory approval to market the AastromReplicell™ System for stem cell therapy. That market is currently dominated by the bone marrow harvest and PBSC collection methods. Our clinical data, although early, suggests that cells expanded in the AastromReplicell™ System using its current process will enable hematopoietic recovery within the time frames currently achieved by bone marrow harvest, however, neutrophil and platelet recovery times may be slower than with PBSC collection methods. In recognition of this, we have begun clinical testing of a procedure that utilizes a combination of PBSCs collected in a single blood apheresis procedure with cells produced in the AastromReplicell™ System. The objectives of this study are to demonstrate that an optimal targeted recovery can be achieved using AastromReplicell™ System-produced cells with a sub-optimal PBSC dose that otherwise would not provide this desired outcome. We are also evaluating techniques and methods to optimize the cells produced in the AastromReplicell™ System to reduce the recovery time of neutrophils and platelets in patients. There can be no assurance that if such procedure optimization does not lead to recovery times equal to or faster than those of PBSC collection methods, such outcome would not have a material adverse affect on our business, financial condition and results of operations. In addition, the bone marrow harvest and PBSC collection methods have been widely practiced for a number of years and the patient costs associated with these procedures have begun to decline. There can be no assurance that the AastromReplicell™ System method, if approved for marketing, will prove to be competitive with these established collection methods on the basis of hematopoietic recovery time, cost or otherwise. We are aware of certain other products manufactured or under development by competitors that are used for the prevention or treatment of certain diseases and health conditions which we have targeted for product development. There can be no assurance that developments by others will not render our product candidates or technologies obsolete or noncompetitive, that we will be able to keep pace with new technological developments or that our product candidates will be able to supplant established products and methodologies in the therapeutic areas that are targeted by us. The foregoing factors could have a material adverse affect on our business, financial condition and results of operations.

Our products under development are expected to address a broad range of existing and new markets. We believe that our stem cell therapy products will, in large part, face competition by existing procedures rather than novel new products. Further, in instances that do not require our patented processes for growing cells, we will face competition for our products from existing manual cell culture techniques, which techniques may be viewed by potential customers as more cost effective than our process. Our competition will be determined in part by the potential indications for which our products are developed and ultimately approved by regulatory authorities. In addition, the first product to reach the market in a therapeutic or preventive area is often at a significant competitive advantage relative to later entrants to the market. Accordingly, the relative speed with which we, or our potential corporate partners, can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market are expected to be important competitive factors. Our competitive position will also depend on our ability to attract and retain qualified scientific and other personnel, develop effective proprietary products, develop and implement production and marketing plans, obtain and maintain patent protection and secure adequate capital resources. We expect our products, if approved for sale, to compete primarily on the basis of product efficacy, safety, patient convenience, reliability, value and patent position.

Employees

As of August 31, 2001, we employed approximately 40 individuals on a full time equivalent basis. A significant number of our management and professional employees have had prior experience with pharmaceutical, biotechnology or medical product companies. None of our employees are covered by collective bargaining agreements, and management considers relations with our employees to be good.

Executive Officers of Aastrom

Our executive officers, and their respective ages as of August 31, 2001, are as follows:

Name	Age	Position
R. Douglas Armstrong, Ph.D.	48	President, Chief Executive Officer and Chairman of the Board of Directors
Brian S. Hampson	44	Vice President Product Development
Bruce W. Husel	43	Vice President Quality Systems and Regulatory Affairs
Audrey H. Hutter	42	Vice President Market Operations
Todd E. Simpson	40	Vice President Finance & Administration, Chief FinancialOfficer, Secretary and Treasurer
Steven N. Wolff, M.D.	52	Vice President Medical Research

R. Douglas Armstrong, Ph.D. joined Aastrom in June 1991 as a director and as its President and Chief Executive Officer. From 1987 to 1991, Dr. Armstrong served in different capacities, including Executive Vice President and Trustee of the La Jolla Cancer Research Foundation (LJCRF), now named the Burnham Institute, a 250-employee scientific research institute located in San Diego, California. Dr. Armstrong received his doctorate in Pharmacology and Toxicology from the Medical College of Virginia, and has held faculty and staff positions at Yale University, University of California, San Francisco, LJCRF and University of Michigan.

Brian S. Hampson joined Aastrom in July 1993 as Director, Product Engineering and became Vice President Product Development in June 2000. He has been a principal leader in the development and engineering of the AastromReplicell™ System. Previously, Mr. Hampson served as Manager, In Vitro Systems at Charles River Laboratories and held other positions after joining that company in January 1986. While at Charles River, he managed a number of programs to develop and commercialize novel bioreactor systems to support large-scale cell culture and biomolecule production. Prior to that, Mr. Hampson held several engineering positions at Corning Incorporated from September 1979 to January 1986, including assignments with KC Biological, a wholly owned subsidiary of Corning at the time. Mr. Hampson received his Bachelor of Science and Master of Engineering degrees in Electrical Engineering from Cornell University.

Bruce W. Husel joined Aastrom in November 1997 as Vice President Quality Systems. From May 1994 to September 1997, Mr. Husel served as Director of Quality Assurance for Sanofi Diagnostics Pasteur, where he led efforts to achieve EN 46001 registration and prepare for CE Marking. From June 1992 to May 1994, Mr. Husel was Director of Quality and Regulatory Affairs for Baxter Anesthesia Division (formerly known as Bard MedSystems). Prior to that, he served as Quality Manager of McGaw, Inc. Mr. Husel received his Bachelor of Business degree in Electrical Engineering from Rice University, an Master of Science degree in Engineering Management from Southern Methodist University and a Master of Business Administration degree in Accounting from the University of Texas at Dallas.

Audrey H. Hutter joined Aastrom in January 2001 as Vice President Market Operations. Prior to joining Aastrom, Ms. Hutter held various sales and marketing positions at Beckman Coulter Diagnostics, most recently as National Manager for Technological and Scientific Marketing for North American Operations. While at Beckman Coulter, she was responsible for the development of strategic marketing and tactical marketing programs for the launch and commercialization of diagnostic medical devices. Previously, Ms. Hutter held management and marketing positions at Schering-Plough Corporation, and at Bristol-Myers Squibb. Ms. Hutter received her Bachelor of Science in Biology and Master of Arts in Germanic Languages degrees from the University of Michigan.

Todd E. Simpson joined Aastrom in January 1996 as Vice President Finance and Administration and Chief Financial Officer and is also Aastrom's Secretary and Treasurer. Prior to that, Mr. Simpson was Treasurer of Integra LifeSciences Corporation, a biotechnology company, which acquired Telios Pharmaceuticals, Inc. in August 1995. Mr. Simpson served as Vice President of Finance and Chief Financial Officer of Telios up until its acquisition by Integra and held various other financial positions at Telios after joining that company in February 1992. Telios was a publicly-held company engaged in the development of pharmaceutical products for the treatment of dermal and ophthalmic wounds, fibrotic disease, vascular disease, and osteoporosis. From August 1983 through February 1992, Mr. Simpson practiced public accounting with the firm of Ernst & Young, LLP. Mr. Simpson is a Certified Public Accountant and received his Bachelor of Science degree in Accounting and Computer Science from Oregon State University. Mr. Simpson has decided to leave Aastrom to pursue other opportunities. Aastrom has begun the process of hiring a new Chief Financial Officer and Mr. Simpson will continue to assist Aastrom during a transition period.

Steven N. Wolff, M.D., joined Aastrom in April 2001 as Vice President Medical Research. Prior to joining Aastrom, Dr. Wolff held various distinguished positions at the Vanderbilt University School of Medicine, most recently as Professor of Medicine in the Division of Hematology/Oncology, and as Director of the Bone Marrow Transplant Program. In addition, Dr. Wolff has served on the National Marrow Donor Program Council from 1995 to 1997, as the Council's President in 1997, and as the Chairman of the Finance Committee. Currently, Dr. Wolff participates as a Board Member for the Lance Armstrong Foundation, having served as its Board President in 1998. Dr. Wolff holds an M.D. from the University of Illinois, with postgraduate training at Vanderbilt University School of Medicine and Washington University School of Medicine, and holds an undergraduate degree from Queens College.

ITEM 2. PROPERTIES

We lease approximately 22,000 square feet of office and research and development space in Ann Arbor, Michigan. While such facilities have previously been leased under a long-term operating lease, we currently lease our facilities under a month-to-month lease. We believe that our facilities are adequate for our current needs. Additional facilities may be required to support expansion for research and development abilities or to assume manufacturing operations that are currently fulfilled through contract manufacturing relationships.

ITEM 3. LEGAL PROCEEDINGS

We are not currently party to any material legal proceedings, although from time to time we may become involved in disputes in connection with the operation of our business.

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

None

PART II

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

Since February 4, 1997 our common stock has been quoted on the Nasdaq National Market under the symbol "ASTM". The following table sets forth the high and low closing prices per share of common stock as reported on the Nasdaq National Market:

Price Range of Common Stock

	High	Low
Year ended June 30, 2000:		
1st Quarter	$1.97	$1.31
2nd Quarter	1.31	.44
3rd Quarter	7.75	.72
4th Quarter	4.31	2.00
Year ended June 30, 2001:		
1st Quarter	4.31	1.53
2nd Quarter	2.78	.81
3rd Quarter	1.59	.78
4th Quarter	2.34	.75

As of August 31, 2001, there were approximately 380 holders of record of the common stock. We have never paid any cash dividends on our common stock and we do not anticipate paying such cash dividends in the foreseeable future. We currently anticipate that we will retain all future earnings, if any, for use in the development of our business.

On June 11, 2001, Aastrom sold an aggregate of 765,381 shares of common stock (for an aggregate purchase price of $7,654) to a single institutional investor upon the exercise of a warrant that had been issued in February 2000. Based upon the representations made in the various purchase and exercise agreements, these shares were sold pursuant to exemptions from registration provided by section 4 (2) of the Securities Act and Regulation D.

ITEM 6. SELECTED FINANCIAL DATA

The statement of operations data for the years ended June 30, 1999, 2000 and 2001 and for the period from March 24, 1989 (Inception) to June 30, 2001 and the balance sheet data at June 30, 2000 and 2001, are derived from, and are qualified by reference to, the audited consolidated financial statements included in this report on Form 10-K and should be read in conjunction with those financial statements and notes thereto. The statement of operations data for the years ended June 30, 1997 and 1998, and the balance sheet data at June 30, 1997, 1998 and 1999, are derived from audited consolidated financial statements not included herein. The data set forth below are qualified by reference to, and should be read in conjunction with, the consolidated financial statements and notes thereto and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year ended June 30,					March 24, 1989 (Inception) to June 30, 2001
	1997	1998	1999	2000	2001	
Statement of Operations Data:						
Revenues:						
Product sales and rentals	$ —	$ —	$ 34,000	$ 169,000	$ 85,000	$ 288,000
Research and development agreements	230,000	3,000	—	—	—	2,020,000
Grants	148,000	246,000	847,000	981,000	814,000	5,031,000
Total revenues	378,000	249,000	881,000	1,150,000	899,000	7,339,000
Costs and expenses:						
Cost of product sales and rentals(1)	—	—	6,000	1,251,000	13,000	1,270,000
Research and development	13,357,000	15,498,000	10,871,000	6,289,000	4,983,000	76,073,000
Selling, general and administrative	1,953,000	2,858,000	2,836,000	3,364,000	2,482,000	20,582,000
Total costs and expenses	15,310,000	18,356,000	13,713,000	10,904,000	7,478,000	97,925,000
Loss from operations	(14,932,000)	(18,107,000)	(12,832,000)	(9,754,000)	(6,579,000)	(90,586,000)
Other income (expense):						
Other income	—	—	1,237,000	—	—	1,237,000
Interest income	676,000	886,000	571,000	364,000	653,000	4,726,000
Interest expense	(32,000)	(12,000)	(4,000)	—	—	(267,000)
Net loss	$(14,288,000)	$(17,233,000)	$(11,028,000)	$ (9,390,000)	$ (5,926,000)	$(84,890,000)
Net loss applicable to common shares	$(14,288,000)	$(21,023,000)	$(11,507,000)	$ (9,598,000)	$ (5,926,000)	
Net loss per common share (basic and diluted)	$ (1.27)	$ (1.57)	$ (.75)	$ (.41)	$ (.17)	
Weighted average number of common shares outstanding	11,228,000	13,363,000	15,342,000	23,344,000	34,030,000	

	June 30,				
	1997	1998	1999	2000	2001
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$17,007,000	$11,212,000	$ 7,528,000	$12,745,000	$10,659,000
Working capital	15,600,000	10,121,000	8,009,000	12,143,000	10,715,000
Total assets	18,410,000	12,374,000	9,540,000	13,437,000	11,905,000
Long-term capital lease obligations	65,000	—	—	—	—
Deficit accumulated during the development stage	(41,313,000)	(58,897,000)	(70,334,000)	(79,932,000)	(85,858,000)
Total shareholders' equity	16,583,000	10,846,000	8,511,000	12,435,000	10,894,000

(1) Cost of product sales and rentals for the year ended June 30, 2000 includes an inventory write off of $1,027,000.

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

Overview

Since Aastrom's inception, we have been in the development stage and engaged in research and product development, conducted principally on our own behalf, but also in connection with various collaborative research and development agreements with others. We commenced our initial pilot-scale product launch in Europe of the AastromReplicell™ Cell Production System (System) in April 1999, but subsequently suspended those activities in October 1999 pending the receipt of additional financing. While these activities are now in process, we do not expect to generate positive cash flows from operations for at least the next several years and then only if more significant product sales commence. Until that time, we expect that our revenue sources will be limited to grant revenue and research funding, milestone payments and licensing fees from potential future corporate collaborators. The timing and amount of such future cash payments and revenues, if any, will be subject to significant fluctuations, based in part on the success of our research activities, the receipt of necessary regulatory approvals, the timing of the achievement of certain other milestones and the extent to which associated costs are reimbursed under grant or other arrangements. A portion of our revenues from product sales will be subject to our obligation to make aggregate royalty payments of up to 2% to certain licensors of our technology. Research and development expenses may fluctuate due to the timing of expenditures for the varying stages of our research, product development and clinical development programs and the availability of resources. Generally, product development expenses have decreased as we have transitioned from prototype-versions to production-level versions of the AastromReplicell™ System. Operating expenses have also decreased over the past year as a result of cost reduction efforts that we have implemented. Clinical development costs are expected to increase as we conduct our U.S. clinical trials, successful completion of which are necessary to

submit for regulatory approvals to market our products in the U.S. Similarly, marketing and other general and administrative expenses are expected to increase in support of European marketing activities. As a result of these and other factors, our results of operations have fluctuated and are expected to continue to fluctuate significantly from year to year and from quarter to quarter and therefore may not be comparable to or indicative of the results of operations for any future periods.

In the two most recent years our net loss has decreased as development activities for our lead product candidate decreased. The scope and size of our operations is typically tied to the availability of capital and other resources. For example, in October 1999, we were forced to implement significant cost reduction measures while we pursued corporate partnering, including merger or acquisition transactions, and sought additional capital. We completed several sales of equity securities in the past two years allowing us to resume our U.S. clinical development program and pilot-scale marketing activities in Europe with targeted medical centers. We need to obtain additional financing and we continue to pursue our financing options.

In order for us to resume more expanded operations, we will need to hire more personnel to address requirements in the areas of product and customer support, research, clinical and regulatory affairs, quality systems, sales and marketing and administration. Our operating expenses are expected to increase as a result. At least until such time as we enter into arrangements providing research and development funding or achieve greater product sales, we will continue to incur net operating losses. As a development-stage company, we have never been profitable and do not anticipate having net income unless and until significant product sales commence, which is unlikely to occur until we obtain significant additional funding. Through June 30, 2001, we have accumulated losses of $84,890,000. There can be no assurance that we will be able to achieve profitability on a sustained basis, if at all, obtain the required funding, or complete a corporate partnering or acquisition transaction.

Results of Operations

Total revenues were $899,000 in 2001, $1,150,000 in 2000, and $881,000 in 1999. Revenues include product sales and rentals of $85,000 in 2001 $169,000 in 2000 and $34,000 in 1999, reflecting the pilot-scale marketing of our lead product, the AastromReplicell™ System. We commenced our initial pilot-scale product launch in Europe of the AastromReplicell™ Cell Production System (System) in April 1999, but subsequently suspended those activities in October 1999 pending the receipt of additional financing. Marketing activities have now been resumed. Grant revenues decreased to $814,000 in 2001 from $981,000 in 2000, and from $847,000 in 1999, reflecting the award of research grants and related research activities, to the extent that such associated costs are reimbursed under the grants. Grant revenues accounted for 91%, 85% and 96% of total revenues for the years ended June 30, 2001, 2000 and 1999, respectively, and are recorded on a cost-reimbursement basis.

Total costs and expenses were $7,478,000 in 2001, $10,904,000 in 2000 and $13,713,000 in 1999. The decrease in costs and expenses during the periods is principally the result of a decrease in research and development expense to $4,983,000 in 2001 from $6,289,000 in 2000 and from $10,871,000 in 1999. These decreases reflect declining development activities for the AastromReplicell™ System. Cost of product sales and rentals were $13,000 in 2001 compared to $1,251,000 in 2000 and $6,000 in 1999, reflecting the pilot-scale European product launch of the AastromReplicell™ System in 1999. Cost of product sales and rentals in 2000 consisted principally of AastromReplicell™ System inventory that was written off in connection with the suspension of marketing activities. Research and development expense includes a charge of $1,100,000 in 2000 and 1999, representing license fee payments pursuant to our supply agreement with Immunex. This license agreement has been extended through March 2003, without further annual renewal payments. General and administrative expenses decreased to $2,482,000 in 2001 from $3,364,000 in 2000, reflecting the planned expense reduction measures previously implemented, but increased in 2000 from $2,836,000 in 1999 reflecting increased finance, legal and other administrative and marketing expenses in support of our product development, research and European activities.

Interest income was $653,000 in 2001, $364,000 in 2000 and $571,000 in 1999. The fluctuations in interest income are due primarily to corresponding changes in the levels of cash, cash equivalents and short-term investments during the periods. Other income for the year ended June 30, 1999 includes $1,237,000 representing a one-time payment that we received in November 1998.

Our net loss was $5,926,000, or $.17 per common share in 2001, $9,390,000, or $.41 per common share in 2000, and $11,028,000, or $.75 per common share in 1999. The computations of net loss per common share in 1999 and 2000 include adjustments for dividends and yields on outstanding preferred stock as well as one-time charges related to the sale of preferred stock. The one-time charges, dividends and yields affect only the computation of net loss per common share and are not included in the net loss for the periods. The decreases in net loss per common share reflect a decreases in the net loss during the period as well as an increase in the number of common shares outstanding resulting from our capital raising activities. We expect to report additional significant net losses until such time as more substantial product sales commence.

We have not generated any profits to date and therefore have not paid any federal income taxes since inception. At June 30, 2001, our Federal tax net operating loss and tax credit carryfowards were $82,600,000 and $2,300,000, respectively, which will expire from 2004 through 2021, if not utilized. In July 1998, we issued shares of 1998 Series I Convertible Preferred Stock which resulted in a change in ownership and an annual limitation of $3,136,000, which applies to losses incurred between October 1993 and July 1998. As of June 2001, the portion of our net operating loss that remains subject to this limitation is approximately $41,000,000. Our ability to utilize our net operating loss and tax credit carryforwards may become subject to further annual limitation in the event of other change in ownership events.

Liquidity and Capital Resources

We have financed our operations since inception primarily through public and private sales of our equity securities, which, from inception through June 30, 2001, have totaled approximately $97 million and, to a lesser degree, through grant funding, payments received under research agreements and collaborations, interest earned on cash, cash equivalents, and short-term investments, and funding under equipment leasing agreements. These financing sources have historically allowed us to maintain adequate levels of cash and other liquid investments.

Our combined cash, cash equivalents and short-term investments totaled $10,659,000 at June 30, 2001, a decrease of $2,086,000 from June 30, 2000. During the year ended June 30, 2001, we raised net proceeds of $4,265,000 through the sale of our equity securities. The primary uses of cash, cash equivalents and short-term investments during the year ended June 30, 2001 included $6,293,000 to finance our operations and working capital requirements, and $58,000 in capital equipment additions.

Our future cash requirements will depend on many factors, including continued scientific progress in our research and development programs, the scope and results of clinical trials, the time and costs involved in obtaining regulatory approvals, the costs involved in filing, prosecuting and enforcing patents, competing technological and market developments and the cost of product commercialization. We do not expect to generate a positive cash flow from operations for at least the next several years due to the expected spending for research and development programs and the cost of commercializing our product candidates. We intend to seek additional funding through research and development, or distribution and marketing, agreements with suitable corporate collaborators, grants and through public or private financing transactions. Successful future operations are subject to several technical and business risks, including our continued ability to obtain future funding, satisfactory product development, obtaining regulatory approval and market acceptance for our products. Based on current funding and anticipated operating activities, we expect that our available cash and expected interest income will be sufficient to finance currently planned activities through at least the end of fiscal year 2002. This estimate is a forward-looking statement based on certain assumptions which could be negatively

impacted by the matters discussed under this heading and under the caption "Business Risks", included herein. We are pursuing additional sources of financing. If we cannot obtain additional funding prior to our current cash reserves being depleted, we will be forced to make substantial reductions in the scope and size of our operations, and may be forced to curtail activities currently planned to be resumed. In order to grow and expand our business, and to introduce our product candidates into the marketplace, we will need to raise additional funds. We will also need additional funds or a collaborative partner, or both, to finance the research and development activities of our product candidates for the expansion of additional cell types. We expect that our primary sources of capital for the foreseeable future will be through collaborative arrangements and through the public or private sale of our debt or equity securities. There can be no assurance that such collaborative arrangements, or any public or private financing, will be available on acceptable terms, if at all, or can be sustained. Several factors will affect our ability to raise additional funding, including, but not limited to, market volatility of our common stock and economic conditions affecting the public markets generally or some portion or all of the technology sector. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our research and development programs, which may have a material adverse affect on our business. See "Business Risks" and "Notes to Consolidated Financial Statements" included herein.

New Accounting Standards

In July 2001, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 141, "Business Combinations" and No. 142, "Goodwill and Other Intangible Assets" which are effective for the Company beginning July 1, 2002. The adoption of SFAS No. 141 and No. 142 are being evaluated by management and are not expected to have a significant impact on the Company's financial position or results of operations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The only financial instruments we maintain are in accounts receivables. We believe that the interest rate risk related to these accounts is not significant. We manage the risk associated with these accounts through periodic reviews of the carrying value for non-collectability and establishment of appropriate allowances in connection with our internal controls and policies. We do not enter into hedging or derivative instruments.

BUSINESS RISKS

Our business is subject to a number of uncertainties, including those discussed below.

If we cannot complete our product development activities successfully, our ability to operate or finance operations will be severely limited.

Commercialization in the United States of our lead product candidate, the AastromReplicell™ Cell Production System, will require additional research and development as well as substantial clinical trials. While we have commenced initial marketing on a very limited basis of the AastromReplicell™ System in Europe, we believe that the United States will be the principal market for our products. We may not be able to successfully complete development of the AastromReplicell™ System or our other product candidates, or successfully market our technologies or product candidates. We and any of our potential collaborators may encounter problems and delays relating to research and development, regulatory approval and intellectual property rights of our technologies and product candidates. Our research and development programs may not be successful, and our cell culture technologies and product candidates may not facilitate the *ex vivo* production of cells with the expected biological activities in humans. Our technologies and product candidates may not prove to be safe and efficacious in clinical trials, and we may not obtain the intended regulatory approvals for our technologies or product candidates and the cells produced in such products. If any of these events occur, we may not have adequate resources to continue operations for the period required to resolve the issue delaying commercialization and we may not be able to raise capital to finance our continued operation during the period required for resolution of that issue.

We cannot be certain that we will be able to raise the required capital to conduct our operations and develop our products.

We will require substantial capital resources in order to conduct our operations and develop our products. In October 1999, we were forced to reduce operations based on our declining level of capital resources and our limited financing alternatives available at that time. Although we have started to restore operating activities, the previous reduction in our operating activities has negatively affected our ability to develop our products and has delayed our product development programs. Based on current funding and anticipated operating activities, we expect that our available cash and expected interest income will be sufficient to finance currently planned activities through at least the end of fiscal year 2002. This is a forward-looking statement and could be negatively affected by funding limitations, the implementation of additional research and development programs and other factors discussed under this heading. We are currently pursuing additional sources of financing. If we cannot obtain additional funding prior to that time, we will be forced to make substantial reductions in the scope and size of our operations, and may be forced to curtail activities that we currently plan to resume. In order to grow and expand our business, and to introduce our product candidates into the marketplace, we will need to raise additional funds. We will also need additional funds or a collaborative partner, or both, to finance the research and development activities of our new product candidates for the production of additional cell types.

Our future capital requirements will depend upon many factors, including:

- continued scientific progress in our research and development programs;
- costs and timing of conducting clinical trials and seeking regulatory approvals and patent prosecutions;
- competing technological and market developments;
- our ability to establish additional collaborative relationships; and
- effective commercialization activities and facility expansions if and as required.

Because of our long-term funding requirements, we may attempt to access the public or private equity markets if and whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. Further, we may enter into financing transactions at rates which are at a substantial discount to market. This additional funding may not be available to us on reasonable terms, or at all. If adequate funds are not available, we may be required to further delay or terminate research and development programs, curtail capital expenditures, and reduce business development and other operating activities.

We must successfully complete our clinical trials to be able to market our products.

To be able to market products in the United States, we must demonstrate, through extensive preclinical studies and clinical trials, the safety and efficacy of our processes and product candidates, together with the cells produced by such processes in such products, for application in the treatment of humans. We are currently conducting clinical trials to demonstrate the safety and biological activity of patient-derived cells produced in the AastromReplicell™ System. Depending on the availability of resources, we intend to commence at least one additional clinical trial to demonstrate the safety and biological activity of umbilical cord blood cells produced in the AastromReplicell™ System. If our clinical trials are not successful, our products may not be marketable.

Our ability to complete our clinical trials in a timely manner depends on many factors, including the rate of patient enrollment. Patient enrollment can vary with the size of the patient population, the proximity of suitable patients to clinical sites, perceptions of the utility of stem cell therapy for the treatment of certain diseases and the eligibility criteria for the study. We have experienced delays in patient accrual in our previous and current clinical trials. If we experience future delays in patient accrual, we could experience increased costs and delays associated with clinical trials which would impair our product development programs and our ability to market our products. Furthermore, the U.S. Food and Drug Administration (FDA) monitors the progress of clinical trials and it may suspend or terminate clinical trials at any time due to patient safety or other considerations.

Failure to obtain and maintain required regulatory approvals would severely limit our ability to sell our products.

We must obtain the approval of the FDA before commercial sales of our product candidates may commence in the United States, which we believe will be the principal market for our products. We may also be required to obtain additional approvals from foreign regulatory authorities to continue or increase our sales activities in those jurisdictions. If we cannot demonstrate the safety, reliability and efficacy of our product candidates, or of the cells produced in such products, we may not be able to obtain required regulatory approvals. Many of the patients enrolled in the clinical trials will have previously undergone extensive treatment which will have substantially weakened the patients and may have irreparably damaged the ability of their blood and immune system to recover. Some patients undergoing the transplant recovery process have died, from causes that were, according to the physicians involved, unrelated to the AastromReplicell™ System procedure, and it is possible that other patients may die or suffer severe complications during the course of either the current or future clinical trials. In addition, patients receiving cells produced with our technologies and product candidates may not demonstrate long-term engraftment in a manner comparable to cells obtained from current stem cell therapy procedures. If we cannot demonstrate the safety or efficacy of our technologies and product candidates, including long-term sustained engraftment, or if one or more patients die or suffer severe complications, the FDA or other regulatory authorities could delay or withhold regulatory approval of our product candidates.

Finally, even if we obtain regulatory approval of a product, that approval may be subject to limitations on the indicated uses for which it may be marketed. Even after granting regulatory approval, the FDA, other regulatory agencies, and governments in other countries continue to review and inspect marketed products, manufacturers and manufacturing facilities. Later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer, including a withdrawal of the product from the market. Further, governmental regulatory agencies may establish additional regulations which could prevent or delay regulatory approval of our products.

Even if we obtain regulatory approvals to sell our products, lack of commercial acceptance would impair our business.

Our product development efforts are primarily directed toward obtaining regulatory approval to market the AastromReplicell™ System as an alternative to, or as an improvement for, the bone marrow harvest and peripheral blood progenitor cell stem cell collection methods. These stem cell collection methods have been widely practiced for a number of years, and our technologies or product candidates may not be accepted by the marketplace as readily as these or other competing processes and methodologies. Additionally, our technologies or product candidates may not be employed in all potential applications being investigated, and any limited applications would limit the market acceptance of our technologies and product candidates and our potential revenues. As a result, even if we obtain all required regulatory approvals, we cannot be certain that our products and processes will be adopted at a level that would allow us to operate profitably.

Failure of third parties to manufacture component parts or provide limited source supplies would impair our new product development and our sales activities.

We rely solely on third parties to manufacture our product candidates and their component parts. We also rely solely on third party suppliers to provide necessary key mechanical components, as well as growth factors and other materials used in the cell expansion process. We would not be able to obtain alternate sources of supply for many of these items on a short-term basis. In October 1999, we suspended manufacturing of our products. While we are in the process of reestablishing our product manufacturing capabilities, we have not yet completed those activities and resumed production of certain components of our product line. If any of our key manufacturers or suppliers fail to perform their respective obligations or if our supply of growth factors, components or other materials is limited or interrupted, we would not be able to conduct clinical trials or market our product candidates on a timely and cost-competitive basis, if at all.

Furthermore, some of the compounds used by us in our current stem cell expansion processes involve the use of animal-derived products. Suppliers or regulatory authorities may limit or restrict the availability of such compounds for clinical and commercial use. Any restrictions on these compounds would impose a potential competitive disadvantage for our products. If we were not able to develop or obtain alternative compounds, our product development and commercialization efforts would be harmed.

Finally, we may not be able to continue our present arrangements with our suppliers, supplement existing relationships, establish new relationships or be able to identify and obtain the ancillary materials that are necessary to develop our product candidates in the future. Our dependence upon third parties for the supply and manufacture of these items could adversely affect our ability to develop and deliver commercially feasible products on a timely and competitive basis.

Our past losses and expected future losses cast doubt on our ability to operate profitably.

We were incorporated in 1989 and have experienced substantial operating losses since inception. As of June 30, 2001, we have incurred net operating losses totaling approximately $85 million. These losses have resulted principally from costs incurred in the research and development of our cell culture technologies and the AastromReplicell™ System, general and administrative expenses, and the prosecution of patent applications. We expect to incur significant operating losses until product sales increase, primarily owing to our research and development programs, including pre-clinical studies and clinical trials, and the establishment of marketing and distribution capabilities necessary to support commercialization efforts for our products. We cannot predict with any certainty the amount of future losses. Our ability to achieve profitability will depend, among other things, on successfully completing the development of our product candidates, obtaining regulatory approvals, establishing manufacturing, sales and marketing arrangements with third parties, and raising sufficient funds to finance our activities. We may not be able to achieve or sustain profitability.

Given our limited internal sales and marketing capabilities, we need to develop collaborative relationships to sell, market and distribute our products.

While we have commenced initial marketing on a limited basis of the AastromReplicell™ System in Europe, we have only limited internal sales, marketing and distribution capabilities. We intend to market our products through collaborative relationships with companies for sales, marketing and distribution capabilities. If we cannot develop and maintain those relationships, we would have only a limited ability to market, sell and distribute our products. Even if we are able to enter into such relationships, they may not succeed or be sustained on a long-term basis, and termination would require us to develop alternate arrangements at a time when we need sales, marketing or distribution capabilities to meet existing demand. For example, in November 1998 Aastrom and COBE BCT terminated a strategic alliance for the worldwide distribution of the AastromReplicell™ System for stem cell therapy and related uses. We are now seeking to enter into other arrangements relating to the development and marketing of our product candidates.

Any changes in the governmental regulatory classifications of our products could prevent, limit or delay our ability to market or develop our products.

The FDA establishes regulatory requirements based on the classification of a product. Although the FDA has indicated it intends to regulate the AastromReplicell™ System for stem cell therapy as a Class III medical device, the FDA may ultimately choose to regulate the AastromReplicell™ System under another category. Because our product development programs are designed to satisfy the standards applicable to Class III medical devices, a change in the regulatory classification would affect our ability to obtain FDA approval of our products. Also, the FDA is in the process of developing its requirements with respect to somatic cell therapy and gene cell therapy products. Until the FDA issues definitive regulations covering our product candidates, the regulatory guidelines or requirements for approval of such product candidates and/or the cells produced by them will continue to be uncertain.

If we do not keep pace with our competitors and with technological and market changes, our products may become obsolete and our business may suffer.

The market for our product is very competitive and is subject to rapid technological changes. Many of our competitors have significantly greater resources, more product candidates and have developed product candidates and processes that directly compete with our products. Our competitors may have developed, or could in the future develop, new technologies that compete with our products or even render our products obsolete. In addition, some recently published studies have suggested that stem cell therapy, which is the current principal market for our SC-I Therapy Kit, may have limited clinical benefit in the treatment of breast cancer, which is a significant portion of the current overall stem cell transplant market. Our products are designed to improve and automate the processes for producing cells used in therapeutic procedures. Even if we are able to demonstrate improved or equivalent results, researchers and practitioners may not use our products and we will suffer a competitive disadvantage. As a result, we may be unable to recover the net book value of our inventory. Finally, to the extent that others develop new technologies that address the targeted application for our products, our business will suffer.

If we cannot attract and retain key personnel, then our business will suffer.

Our success depends in large part upon our ability to attract and retain highly qualified scientific and management personnel. We face competition for such personnel from other companies, research and academic institutions and other entities. For example, we recently announced the resignation of our Vice President Finance & Administration and Chief Financial Officer who left the company to pursue other opportunities. Further, in an effort to conserve financial resources, we have been forced to implement reductions in our work force on two separate occasions. As a result of these and other factors, we may not be successful in hiring or retaining key personnel.

The warrants have the potential for substantial dilution.

We have warrants to purchase 2,614,386 shares of common stock at $1.58 per share and options to purchase 2,047,862 shares at a weighted average price of $2.03 per share outstanding. Holders of common stock could therefore experience dilution of their investment upon exercise of these warrants and options.

Our stock price has been volatile and future sales of substantial numbers of our shares could have an adverse affect on the market price of our shares.

The market price of shares of our common stock has been volatile. The price of our common stock may continue to fluctuate in response to a number of events and factors, such as:

- clinical trial results;
- the amount of our cash resources and our ability to obtain additional funding;
- announcements of research activities, business developments, technological innovations or new products by us or our competitors;
- changes in government regulation;
- disputes concerning patents or proprietary rights;
- changes in our revenues or expense levels;
- public concern regarding the safety, efficacy or other aspects of the products or methodologies we are developing; and
- changes in potential recommendations by securities analysts.

Any of these events may cause the price of our shares to fall, which may adversely affect our business and financing opportunities. In addition, the stock market in general and the market prices for biotechnology companies in particular have experienced significant volatility that often has been unrelated to the operating performance or financial conditions of such companies. These broad market and industry fluctuations may adversely affect the trading price of our stock, regardless of our operating performance or prospects. For example, within the last year, our stock price has experienced a day where it traded at approximately twice the previous day's closing price and another day when it dropped by over 20% from the previous day's closing price.

In addition, sales, or the possibility of sales, of substantial numbers of shares of common stock in the public market could adversely affect prevailing market prices of shares of common stock. Our employees hold a significant number of options to purchase shares, many of which are presently exercisable. Employees may exercise their options and sell shares shortly after such options become exercisable, particularly if they need to raise funds to pay for the exercise of such options or to satisfy tax liabilities that they may incur in connection with exercising their options.

If our patents and proprietary rights do not provide substantial protection, then our business and competitive position will suffer.

Our success depends in large part on our ability to develop or license and protect proprietary products and technologies. However, we cannot be assured that patents will be granted on any of our pending or future patent applications. We also cannot be assured that the scope of any of our issued patents will be sufficiently broad to offer meaningful protection. In addition, our issued patents or patents licensed to us could be successfully challenged, invalidated or circumvented so that our patent rights would not create an effective competitive barrier. Furthermore, we rely on licenses granted by the University of Michigan for certain of our patent rights. If we breach such agreements or otherwise fail to comply with such agreements, or if such agreements expire or are otherwise terminated, we may lose our rights under the patents held by the University of Michigan. We also rely on trade secrets and unpatentable know-how that we seek to protect, in part, by confidentiality agreements with our employees, consultants, suppliers and licensees. These agreements may be breached, and we might not have adequate remedies for any breach. If this were to occur, our business and competitive position would suffer.

Intellectual property litigation could harm our business.

Our success will also depend in part on our ability to develop commercially viable products without infringing the proprietary rights of others. Although we have not been subject to any filed infringement claims, other patents could exist or could be filed which would prohibit or limit our ability to market our products or maintain our competitive position. In the event of an intellectual property dispute, we may be forced to litigate. Intellectual property litigation would divert management's attention from developing our products and would force us to incur substantial costs regardless of whether we are successful. An adverse outcome could subject us to significant liabilities to third parties, and force us to curtail or cease the development and sale of our products and processes.

The market for our products will be heavily dependent on third party reimbursement policies.

Our ability to successfully commercialize our product candidates will depend on the extent to which government healthcare programs, such as Medicare and Medicaid, as well as private health insurers, health maintenance organizations and other third party payors will pay for our products and related treatments. Reimbursement by third-party payors depends on a number of factors, including the payor's determination that use of the product is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Reimbursement in the United States or foreign countries may not be available or maintained for any of our product candidates. If we do not obtain approvals for adequate third-party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our investment in product development. Any limits on reimbursement available from third-party payors may reduce the demand for, or negatively affect the price of, our products. For example, recently published studies have suggested that stem cell transplantation in breast cancer, which constitutes a significant portion of the overall stem cell therapy market, may have limited clinical benefit. The market for our products would be negatively affected by lack of reimbursement for these procedures by insurance payors.

Potential product liability claims could affect our earnings and financial condition.

We face an inherent business risk of exposure to product liability claims in the event that the use of the AastromReplicell™ System during research and development efforts, including clinical trials, or after commercialization results in adverse affects. As a result, we may incur significant product liability exposure, which could exceed existing insurance coverage. We may not be able to maintain adequate levels of insurance at reasonable cost and/or reasonable terms. Excessive insurance costs or uninsured claims would increase our operating loss and affect our financial condition.

Our corporate documents and Michigan law contain provisions that may make it more difficult for us to be acquired.

Our board of directors has the authority, without shareholder approval, to issue additional shares of preferred stock and to fix the rights, preferences, privileges and restrictions of these shares without any further vote or action by our shareholders. This authority, together with certain provisions of our charter documents, may have the affect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire control of our company. This affect could occur even if our shareholders consider the change in control to be in their best interest.

Our stock may be delisted from Nasdaq that could affect its market price and liquidity.

We are required to meet certain financial tests (including, but not limited to, a minimum bid price of our common stock of $1.00 and $4 million in tangible net worth) to maintain the listing of our common stock on the Nasdaq National Market. Within the last year, our common stock price has fallen below the minimum level for some periods and during other periods our tangible net worth has been below the amount required. In the future, our stock price or tangible net worth may fall below the Nasdaq requirements, or we may not comply with other listing requirements, with the result being that our common stock might be delisted. If that happened the market price and liquidity of our common stock would be impaired. Further, the National Association of Securities Dealers has recently implemented a change in the minimum listing requirements to include a new $10 million minimum net equity requirement. This change replaces the minimum net worth requirement and becomes effective in November 2002. The result of such a change, or other changes, may be that it will become more difficult for us to maintain compliance with the listing standards, the result of which would be that our stock may be delisted.

Forward-looking statements

This report contains certain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act. These forward-looking statements include statements regarding:

- uncertainties related to potential strategic collaborations with others;
- future capital needs and uncertainty of additional funding;
- uncertainties related to product development and marketability;
- uncertainties related to clinical trials;
- manufacturing and supply uncertainties and dependence on third parties;
- anticipation of future losses;
- limited sales and marketing capabilities;
- uncertainty of regulatory approval and extensive government regulation;
- competition and technological change;
- uncertainty regarding patents and proprietary rights;
- no assurance of third party reimbursement; and
- potential product liability and availability of insurance.

These statements are subject to risks and uncertainties, including those set forth in this Business Risks section, and actual results could differ materially from those expressed or implied in these statements. All forward-looking statements included in this Report on Form 10-K are made as of the date hereof. We assume no obligation to update any such forward-looking statement or reason why actual results might differ.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

REPORT OF INDEPENDENT ACCOUNTANTS

To the Board of Directors and Shareholders of
Aastrom Biosciences, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of shareholders' equity and of cash flows present fairly, in all material respects, the consolidated financial position of Aastrom Biosciences, Inc. (a development stage company) at June 30, 2000 and 2001, and the results of its operations and its cash flows for each of the three years in the period ended June 30, 2001, and for the period from March 24, 1989 (Inception) to June 30, 2001, in conformity with accounting principles generally accepted in the United States of America. 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 of these statements in accordance with auditing standards generally accepted in the United States of America which 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, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for the opinion expressed above.

PRICEWATERHOUSECOOPERS LLP

Minneapolis, MN

August 10, 2001, except for Note 9,
which is as of September 5, 2001

AASTROM BIOSCIENCES, INC.
(a developing stage company)

CONSOLIDATED BALANCE SHEETS

	June 30, 2000	June 30, 2001
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 2,064,000	$10,659,000
Short-term investments	10,681,000	—
Receivables	242,000	129,000
Inventory	—	725,000
Other current assets	158,000	213,000
Total current assets	13,145,000	11,726,000
PROPERTY, NET	292,000	179,000
Total assets	$13,437,000	$11,905,000
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable and accrued expenses	$ 837,000	$ 856,000
Accrued employee expenses	165,000	155,000
Total current liabilities	1,002,000	1,011,000
COMMITMENTS (Note 6)		
SHAREHOLDERS' EQUITY:		
Common Stock, no par value; shares authorized—60,000,000; shares issued	92,367,000	96,752,000

and outstanding—33,607,659 and 37,681,235, respectively		
Deficit accumulated during the development stage	(79,932,000)	(85,858,000)
Total shareholders' equity	12,435,000	10,894,000
Total liabilities and shareholders' equity	$13,437,000	$11,905,000

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(a development stage company)

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year ended June 30,			March 24, 1989 (Inception) to June 30, 2001
	1999	2000	2001	
REVENUES:				
Product sales and rentals	$ 34,000	$ 169,000	$ 85,000	$ 288,000
Research and development agreements	—	—	—	2,020,000
Grants	847,000	981,000	814,000	5,031,000
Total revenues	881,000	1,150,000	899,000	7,339,000
COSTS AND EXPENSES:				
Cost of product sales and rentals	6,000	1,251,000	13,000	1,270,000
Research and development	10,871,000	6,289,000	4,983,000	76,073,000
Selling, general and administrative	2,836,000	3,364,000	2,482,000	20,582,000
Total costs and expenses	13,713,000	10,904,000	7,478,000	97,925,000
LOSS FROM OPERATIONS	(12,832,000)	(9,754,000)	(6,579,000)	(90,586,000)
OTHER INCOME (EXPENSE):				
Other income	1,237,000	—	—	1,237,000
Interest income	571,000	364,000	653,000	4,726,000
Interest expense	(4,000)	—	—	(267,000)
Total other income	1,804,000	364,000	653,000	5,696,000
NET LOSS	$ (11,028,00)	$ (9,390,000)	$ (5,926,000)	$(84,890,000)
COMPUTATION OF NET LOSS APPLICABLE TO COMMON SHARES:				
Net loss	$ (11,028,00)	$ (9,390,000)	$ (5,926,000)	
Dividends and yields on preferred stock	(409,000)	(208,000)	—	
Charge related to issuance of preferred stock	(70,000)	—	—	
Net loss applicable to common shares	$(11,507,000)	$ (9,598,000)	$ (5,926,000)	
NET LOSS PER COMMON SHARE (Basic and Diluted)	$ (.75)	$ (.41)	$ (.17)	
Weighted average number of common shares outstanding	15,342,000	23,344,000	34,030,000	

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC
(in development stage company)

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY

Preferred Stock		Common Stock		Deficit accumulated during the development stage	Accumulated other comprehensive income	Total Shareholders' Equity
Shares	Amount	Shares	Amount			

BALANCE, MARCH 24, 1989 (Inception)	—	$ —	—	$ —	$ —	$ —	$ —
Net loss					(58,546,000)		(58,546,000)
Unrealized gains on investments						4,000	4,000
Comprehensive loss							(58,542,000)
Issuance of common stock for cash, services and license rights			743,218	1,177,000			1,177,000
Issuance of Series A through Series E Preferred Stock for cash, net of issuance costs of $342,000	9,451,766	34,218,000					34,218,000
Issuance of Series E Preferred Stock at $17.00 per share	205,882	3,500,000		(3,500,000)			—
Exercise of stock options			1,507,408	202,000			202,000
Issuance of Stock Purchase Rights for cash in September 1995 and March 1996				3,500,000			3,500,000
Principal payment received under shareholder note receivable				31,000			31,000
Initial public offering of common stock at $7.00 per share, net of issuance costs of $2,865,000			3,250,000	19,885,000			19,885,000
Conversion of preferred stock	(9,657,648)	(37,718,000)	8,098,422	37,718,000			—
Compensation expense related to stock options granted				518,000			518,000
Issuance of 5.5% Convertible Preferred Stock at $5.00 per share, net of issuance costs of $1,070,000	2,200,000	9,930,000					9,930,000
Dividends on preferred stock			72,940	351,000	(351,000)		—
Repurchase and retirement of Common Shares outstanding			(32,171)	(73,000)			(73,000)
BALANCE, JUNE 30, 1998	2,200,000	9,930,000	13,639,817	59,809,000	(58,897,000)	4,000	10,846,000
Net loss					(11,028,000)		(11,028,000)
Unrealized losses on investments						(4,000)	(4,000)
Comprehensive loss							(11,032,000)
Dividend and yields on preferred stock		258,000	75,628	151,000	(409,000)		—
Exercise of stock options			24,043	28,000			28,000
Issuance of 1998 Series I Convertible Preferred Stock at $1,000 per share, net of issuance costs of $460,000	5,000	4,540,000	40,404	149,000			4,689,000
Issuance of 1999 Series III Convertible Preferred Stock at $1,000 per share, net of issuance costs of $280,000	3,000	2,720,000	49,994	90,000			2,810,000
Issuance of common stock			451,906	1,159,000			1,159,000
Conversion of preferred stock	(2,201,000)	(10,860,000)	2,698,369	10,860,000			—
Compensation expense related to stock options granted				11,000			11,000
BALANCE, JUNE 30, 1999	7,000	6,588,000	16,980,161	72,257,000	(70,334,000)	—	8,511,000
Net loss and comprehensive loss					(9,390,000)		(9,390,000)
Dividend and yields on preferred stock		208,000			(208,000)		—
Exercise of stock options and warrants			405,753	409,000			409,000
Conversion of preferred stock	(7,000)	(6,796,000)	10,956,918	6,796,000			—
Compensation expense related to stock options granted				5,000			5,000
Issuance of common stock, net of issuance costs of $200,000			5,264,827	12,900,000			12,900,000
BALANCE, JUNE 30, 2000	—	—	33,607,659	92,367,000	(79,932,000)	—	12,435,000
Net loss and comprehensive loss					(5,926,000)		(5,926,000)
Exercise of stock options and issuance of stock under Employee Stock Purchase Plan			244,600	246,000			246,000
Exercise of stock purchase warrant			765,381	8,000			8,000
Compensation expense related to stock options granted			—	120,000			120,000
Issuance of common stock, net of issuance costs of $39,000			3,063,595	4,011,000			4,011,000
BALANCE, JUNE 30, 2001	—	$ —	37,681,235	$96,752,000	$(85,858,000)	$ —	$10,894,000

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(a development stage company)

CONSOLIDATED STATEMENTS OF CASH FLOW

	Year ended June 30,			March 24, 1989 (Inception) to June 30, 2001
	1999	2000	2001	
OPERATING ACTIVITIES:				
Net loss	$(11,028,000)	$ (9,390,000)	$ (5,926,000)	$(84,890,000)

Adjustments to reconcile net loss to net cash used for operating activities:				
Depreciation and amortization	296,000	346,000	171,000	3,201,000
Loss on property held for resale	—	—	—	110,000
Amortization of discounts and premiums on investments	(70,000)	(21,000)	(69,000)	(543,000)
Stock compensation expense	11,000	5,000	120,000	664,000
Write down of inventory	—	1,027,000	—	1,027,000
Stock issued pursuant to license agreement	1,100,000	1,100,000	—	3,300,000
Changes in assets and liabilities:				
Receivables	54,000	(129,000)	113,000	(153,000)
Inventory	(1,144,000)	117,000	(725,000)	(1,752,000)
Other current assets	17,000	95,000	(55,000)	(213,000)
Accounts payable and accrued expenses	(477,000)	1,000	19,000	856,000
Accrued employee expenses	43,000	(28,000)	(10,000)	155,000
Net cash used for operating activities	(11,198,000)	(6,877,000)	(6,362,000)	(78,238,000)
INVESTING ACTIVITIES:				
Organizational costs	—	—	—	(73,000)
Purchase of short-term investments	(1,000,000)	(10,660,000)	(1,500,000)	(56,624,000)
Maturities of short-term investments	10,200,000	—	12,250,000	57,167,000
Capital purchases	(73,000)	(136,000)	(58,000)	(2,643,000)
Proceeds from sale of property held for resale	—	—	—	400,000
Net cash provided by (used for) investing activities	9,127,000	(10,796,000)	10,692,000	(1,773,000)
FINANCING ACTIVITIES:				
Issuance of preferred stock	7,499,000	—	—	51,647,000
Issuance of common stock	87,000	12,209,000	4,265,000	36,715,000
Repurchase of common stock	—	—	—	(49,000)
Payments received for stock purchase rights	—	—	—	3,500,000
Payments received under shareholder notes	—	—	—	31,000
Principal payments under capital lease obligations	(65,000)	—	—	(1,174,000)
Net cash provided by financing activities	7,521,000	12,209,000	4,265,000	90,670,000
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	5,450,000	(5,464,000)	8,595,000	10,659,000
CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD	2,078,000	7,528,000	2,064,000	—
CASH AND CASH EQUIVALENTS AT END OF PERIOD	$ 7,528,000	$ 2,064,000	$10,659,000	$ 10,659,000
SUPPLEMENTAL CASH FLOW INFORMATION:				
Interest paid	$ 4,000	$ —	$ —	$ 267,000
Additions to capital lease obligations	$ —	$ —	$ —	$ 1,174,000

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(a development stage company)

NOTES TO CONSOLIDATED FINANCIAL STATMENTS

1. Organization and Summary of Significant Accounting Policies

Aastrom Biosciences, Inc. (Aastrom) was incorporated in March 1989 (Inception), began employee-based operations in 1991, and is in the development stage. The Company operates its business in one reportable segment—research and product development, conducted both on its own behalf and in connection with various collaborative research and development agreements with others, involving the development and sale of processes and products for the *ex vivo* production of human cells for use in cell and *ex vivo* gene therapy.

Successful future operations are subject to several technical and business risks, including satisfactory product development, obtaining regulatory approval and market acceptance for its products and the Company's continued ability to obtain future funding.

The Company is subject to certain risks related to the operation of its business and development of its products and product candidates. While the Company's fiscal year 2002 capital requirements have been met, it will need to raise additional funds in order to complete its product development programs and commercialize its first product candidates. The Company cannot be certain that such funding will be available on favorable terms, if at all. Some of the factors that will impact the Company's ability to raise additional capital and its overall success include, the rate and degree of progress for its product development programs, the liquidity and volatility of its equity securities, regulatory and manufacturing requirements and uncertainties, technological developments by competitors and other factors. If the Company cannot raise such funds, it may not be able to develop or enhance products, take advantage of future opportunities, or respond to competitive pressures or unanticipated requirements, which would negatively impact its business, financial condition and results of operations.

Significant Revenue Relationships—One company accounted for 24% of total revenues for the period from Inception to June 30, 2001. Grant revenues consist of grants sponsored by the U.S. government.

Principles of Consolidation—The consolidated financial statements include the accounts of Aastrom and its wholly-owned subsidiary, Zellera AG (Zellera) which is located in Berlin, Germany, (collectively, the Company). All significant inter-company transactions and accounts have been eliminated in consolidation. As of June 30, 2001, Zellera has only limited operations and is not currently a significant component of the consolidated financial statements.

Cash and Cash Equivalents—Cash and cash equivalents include cash and short-term investments with original maturities of three months or less.

Short-Term Investments—Short-term investments consist of U.S. government securities and commercial paper with original maturities of over three months and less than one year. Short-term investments are classified as available-for-sale, and are presented at market value, with unrealized gains and losses on investments reflected as a component of shareholders' equity.

Diversity of Credit Risk—The Company invests its excess cash in U.S. government securities and commercial paper, maintained in U.S. financial institutions, and has established guidelines relative to diversification and maturities in an effort to maintain safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates. The Company has not experienced any significant realized losses on its cash equivalents or short-term investments.

Inventory—Inventory is valued at the lower of cost (specific identification using first in, first out) or market and consists primarily of finished components of the Company's products. During the year ended June 30, 2000, a significant portion of inventory was written off as the result of the Company suspending its European marketing activities. Inventory as of June 30, 2001 includes $528,000 in non-refundable deposits placed with suppliers that relate to the manufacture of the Company's products.

Property—Property is recorded at cost and depreciated or amortized using the straight-line method over the estimated useful life of the asset (primarily three to five years) or the lease term, whichever is shorter.

Revenue Recognition—Revenue from grants and research agreements is recognized on a cost reimbursement basis consistent with the performance requirements of the related agreement. Revenue from product sales is recognized when title to the products transfers to customers and there are no remaining obligations that will affect the customer's final acceptance of the sale. Revenue from achievement of milestone events is recognized when the funding party agrees that the scientific or clinical results stipulated in the agreement have been met. Revenue from licensing fees under licensing agreements is recognized as revenue when there are no future performance obligations remaining with respect to such fees.

Research and Development Costs—Research and development costs are expensed as incurred. Such costs and expenses related to programs under collaborative agreements with other companies totaled $1,645,000 for the period from Inception to June 30, 2001.

Stock Compensation—The Company has adopted the disclosure provisions of Statement of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation" (SFAS 123). As permitted by SFAS 123, the Company continues to apply Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees," (APB 25) and related interpretations and does not recognize compensation expense for its employee stock-based compensation plans as allowed by SFAS 123.

Income Taxes—The Company recognizes deferred tax assets and liabilities for the differences between the carrying amounts and the tax basis of assets and liabilities, as well as net operating loss and tax credit carryforwards. Additionally, the Company establishes a valuation allowance to reflect the likelihood of realization of deferred tax assets.

Net Loss Per Common Share—Net loss per common share is computed using the weighted-average number of common shares outstanding during the period. Common equivalent shares are not included in the per share calculation where the affect of their inclusion would be anti-dilutive. The aggregate number of common equivalent shares that have been excluded from the computations of net loss per common share for the periods ended June 30, 1999, 2000 and 2001 is approximately 1,377,000, 2,390,000 and 4,662,000, respectively. The computations of net loss per common share for the years ended June 30, 1999 and 2000 reflect dividends and yields on outstanding preferred stock which affect only the computation of net loss per common share and are not included in the computation of net loss for the period.

Use of Estimates—The preparation of financial statements in accordance with generally accepted accounting principles requires management to make estimates that affect the amounts reported in the financial statements and disclosures made in the accompanying notes to financial statements. Actual results could differ from those estimates.

Financial Instruments—The Company evaluates the fair value of those assets and liabilities identified as financial instruments and estimates that the fair value of such financial instruments generally approximates the carrying value in the accompanying financial statements. Fair values have been determined through information obtained from market sources and management estimates.

Long-Lived Assets—The Company evaluates the impairment of long-lived assets and long-lived assets to be disposed of whenever events or changes in circumstances indicate that the carrying amount of those assets may not be recoverable. No significant impairment losses have been identified by the Company for any of the periods presented in the accompanying financial statements.

New Accounting Standards—In July 2001, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 141, "Business Combinations" and No. 142, "Goodwill and Other Intangible Assets" which are effective for the Company beginning July 1, 2001 and 2002, respectively. The adoption of SFAS No. 141 and No. 142 are being evaluated by management and are not expected to have a significant impact on the Company's financial position or results of operations.

2. Selected Balance Sheet Information

Short-Term Investments All short-term investments are available-for-sale and have maturities of one year or less and are summarized as follows:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
June 30, 2000:				
U.S. Government Securities	$ 5,431,000	$ —	$ —	$ 5,431,000
Commercial Paper	5,250,000	—	—	5,250,000

	$10,681,000	$ —	$ —	$10,681,000

Receivables—Receivables are presented, net of allowance for doubtful accounts of $0, $94,000 and $34,000 at June 30, 1999, 2000 and 2001, respectively.

Property—Property consists of the following:

	June 30,	
	2000	2001
Machinery and equipment	$1,483,000	$1,381,000
Office equipment	886,000	918,000
Leasehold improvements	622,000	622,000
Equipment under lease	120,000	120,000
	3,111,000	3,041,000
Less accumulated depreciation and amortization	(2,819,000)	(2,862,000)
	$ 292,000	$ 179,000

Accounts Payable and Accrued Expenses—Accounts payable and accrued expenses consists of the following:

	June 30,	
	2000	2001
Accounts payable	$100,000	$257,000
Accrued expenses:		
Clinical studies	118,000	139,000
Professional services	55,000	49,000
Manufacturing and engineering	444,000	277,000
Deferred revenue	—	80,000
Other	120,000	54,000
	$837,000	$856,000

3. Shareholders' Equity

Stock Option Plans—The Company has various stock option plans (Option Plans) and agreements that provide for the issuance of nonqualified and incentive stock options to acquire up to 6,049,927 shares of common stock. Such options may be granted by the Company's Board of Directors to certain of the Company's employees, directors and consultants. The exercise price of incentive stock options shall not be less than the fair market value of the shares on the date of grant. In the case of individuals who are also holders of 10% or more of the outstanding shares of common stock, the exercise price of incentive stock options shall not be less than 110% of the fair market value of the shares on the date of grant. The exercise price of non-qualified stock options shall not be less than 85% of the fair market value on the date of grant. Options granted under these plans expire no later than ten years from the date of grant and generally become exercisable ratably over a four-year period following the date of grant.

Under the Company's outside directors' stock option plan, non-qualified options to purchase 10,000 shares of common stock are granted to each outside director on the day following the Annual Shareholders' meeting or upon their appointment as a director. These options generally vest over a one-year period and expire ten years after the date of grant.

As allowed by SFAS 123, the Company does not recognize compensation expense on stock options granted. If the Company had elected to recognize compensation expense based upon the fair value at the grant dates for stock option awards granted in 1999, 2000 and 2001, in accordance with SFAS No. 123, the pro forma net loss and net loss per common share would be as follows.

	Year ended June 30,		
	1999	2000	2001
Net loss:			
As reported	$11,028,000	$9,390,000	$5,926,000
Pro forma	11,935,000	9,829,000	6,976,000
Net loss per common share:			
As reported	$ (.75)	$ (.41)	$ (.17)
Pro forma	(.81)	(.43)	(.21)

The fair value of options was estimated at the date of grant using the Black-Scholes option pricing model with the following assumptions;

	Year ended June 30,		
	1999	2000	2001
Dividend rate	None	None	None

Expected stock price volatility	40%	80%	100%
Risk-free interest rate	4.5%–5.8%	5.8%–6.3%	4.8%–5.9%
Expected life of options	4 years	1–4 years	4 years

The weighted average fair value of options granted during the years ended June 30, 1999, 2000 and 2001 was $1.33, $.43 and $1.93 per share, respectively.

The following table summarizes option activity:

	Options Outstanding	Options Available for Grant Under Option Plans	Weighted Average Exercise Price Per Share	Options Exercisable at Period End
March 24, 1989 (Inception)				
Options authorized	—	2,999,927		
Options canceled	(425,575)	425,575	$3.09	
Options granted	3,095,501	(3,095,501)	$2.52	
Options exercised	(1,507,408)	—	$ .98	
Balance, June 30, 1998	1,162,518	330,001	$5.12	593,930
Options canceled	(569,881)	569,881	$6.40	
Options granted	738,700	(638,700)	$3.12	
Options exercised	(24,043)	—	$1.18	
Balance, June 30, 1999	1,307,294	261,182	$3.60	729,786
Options authorized	—	1,400,000		
Options canceled	(1,091,612)	991,612	$3.64	
Options granted	1,058,500	(1,058,500)	$1.02	
Options exercised	(86,126)	—	$1.72	
Balance, June 30, 2000	1,188,056	1,594,294	$1.30	1,000,224
Options authorized	—	1,550,000		
Options canceled	(44,852)	44,852	$2.57	
Options granted	1,134,700	(1,134,700)	$2.50	
Options exercised	(230,042)	—	$ .99	
Balance, June 30, 2001	2,047,862	2,054,446	$2.03	880,171

The following table summarizes information about stock-based compensation plans as of June 30, 2001:

Range of Exercise Prices	Number of Options Outstanding	Remaining Contractual Life-years	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price of Exercisable Options
$ .30 – $ .94	854,063	8.8	$ .84	627,953	$ .84
$1.20 – $1.91	119,499	7.9	$1.55	63,243	$1.48
$2.44 – $2.88	69,700	8.6	$2.65	28,563	$2.68
$2.94 – $3.56	989,600	9.0	$3.01	145,412	$3.37
$4.75 – $7.00	15,000	6.2	$5.67	15,000	$5.67
	2,047,862		$2.03	880,171	$1.44

Effective July 1, 2000, the Company adopted Financial Accounting Standards Board Interpretation Number 44 to APB 25 (Interpretation No. 44) as it relates to options to purchase 759,000 shares of common stock issued by the Company in December 1999. As a result, a charge to expense is recorded for subsequent increases in the market price of the Company's common stock above $2.41. This charge continues until such options have been exercised, forfeited or otherwise expire. During the year ended June 30, 2001, a charge of $120,000 was recorded with respect to these stock options and is included in research and development expense. At June 30, 2001, options to purchase 566,000 shares remain outstanding.

Employee Stock Purchase Plan—The Company has an employee stock purchase plan under which eligible employees can purchase common stock, at a discount to the market price, through payroll deductions up to 10% of the employees base compensation, subject to certain limitations, during sequential 24-month offering periods. Each offering period is divided into four consecutive six-month purchase periods beginning on March 1 and September 1 of each year. Unless otherwise provided by the Board of Directors prior to the commencement of an offering period, the price at which stock is purchased under the plan for such offering period is equal to 85% of the lesser of the fair market value of the common stock on the first day of such offering period or the last day of the purchase period of such offering period. During the years ended June 30, 1999, 2000 and 2001, 26,835 shares, 19,627 shares and 14,558 shares, respectively, of common stock were purchased under this plan.

Stock Purchase Warrants—In connection with the sale of common stock in February 2000, the Company issued a three-year warrant that is exercisable into 2,614,386 shares of common stock at an exercise price of $1.58. The warrant contains an anti-dilution provision that may be triggered by future financings of the Company at prices below the exercise price. The warrant is subject to early termination if the closing bid price (as defined) of Aastrom's common stock exceeds $7.39 per share for ten consecutive trading days.

Common Shares Reserved—As of June 30, 2001, the Company has reserved shares of common stock for future issuance as follows:

Issuance under stock option and stock purchase plans	4,277,388
Issuance under stock purchase warrants	2,614,386
	6,891,774

No cash dividends have ever been declared or paid; however, during the year ended June 30, 1999, the Company issued 75,628 shares of common stock valued at $151,000 in payment of the dividends on the 5.5% Convertible Preferred Stock.

4. Income Taxes

Deferred tax assets consist of the following:

	June 30,	
	2000	2001
Net operating loss carryforwards	$26,510,000	$28,900,000
Tax credits and other	2,787,000	2,637,000
Gross deferred tax assets	29,297,000	31,537,000
Valuation allowance	(29,297,000)	(31,537,000)
	$ —	$ —

Due to the historical losses incurred by the Company, a full valuation allowance for deferred tax assets has been provided. If the Company achieves profitability, these deferred tax assets may be available to offset future income taxes. The valuation allowance as of June 30, 1999 was $26,028,000.

At June 30, 2001, the Company's Federal tax net operating loss and tax credit carryfowards were $82,600,000 and $2,300,000, respectively, which will expire from 2004 through 2021, if not utilized. In July 1998, the Company issued shares of 1998 Series I Convertible Preferred Stock which resulted in a change in ownership and an annual limitation of $3,136,000, which applies to losses incurred between October 1993 and July 1998. As of June 2001, the portion of the Company's net operating loss that remains subject to this limitation is approximately $41 million. The Company's ability to utilize its net operating loss and tax credit carryforwards may become subject to further annual limitation in the event of other change in ownership events.

5. Licenses, Royalties and Collaborative Agreements:

University of Michigan—In August 1989, the Company entered into a research agreement with the University of Michigan (the University). In March 1992, and as provided for under the research agreement, the Company also entered into a license agreement for the technology developed under the research agreement. The license agreement, as amended, provides for a royalty to be paid to the University equal to 2% of net sales of products containing the licensed technology sold by the Company.

Manufacture, Supply and Other Agreements—The Company has entered into various agreements relating to the manufacture of its products and the supply of certain components. Pursuant to one such agreement, the Company made annual renewal payments of $1,000,000, due in advance, in March of each year during the initial term of the agreement, which ended in 2001. The renewal fees due in March 1999 and 2000 were paid through this issuance of common stock valued at $1,100,000 each, which is included in research and development expense. The license agreement has been extended for an additional two-year term, subject to further extension, with no additional annual renewal fees due.

Other income for the year ended June 30, 1999 includes $1,237,000 reflecting a one time payment received by the Company in December 1998 relating to the termination of a marketing and distribution agreement.

6. Commitments

As of June 30, 2001, the Company leases its facility under a month-to-month operating lease. Rent expense for the years ended June 30, 1999, 2000 and 2001, was $560,000, $485,000 and $495,000, respectively, and $3,314,000 for the period from Inception to June 30, 2001.

7. Employee Savings Plan

The Company has a 401(k) plan that allows participating employees to contribute up to 15% of their salary, subject to annual limits and minimum qualifications. The Board may, at its sole discretion, approve Company contributions. Through June 30, 2001, the Company has made no contributions to the plan.

8. Quarterly Financial Data (Unaudited)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Fiscal Year
Revenues	$ 167,000	$ 295,000	$ 191,000	$ 246,000	$ 899,000
Loss from operations	(1,615,000)	(1,094,000)	(1,863,000)	(2,007,000)	(6,579,000)
Net loss	(1,406,000)	(916,000)	(1,715,000)	(1,889,000)	(5,926,000)
Net loss per common share	(.04)	(.03)	(.05)	(.05)	(.17)

9. Subsequent Events

During the period from July 1, 2001 through August 31 2001, the Company has issued 4,345,182 shares of its common stock for cash proceeds of approximately $6,500,000.

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

FINANCIAL DISCLOSURE

There are none to report.

PART III

Certain information required by Part III is omitted from this Report, and is incorporated by reference to our definitive Proxy Statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with our 2001 Annual Meeting of Shareholders to be held on November 14, 2001.

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information relating to our directors is incorporated by reference to the Proxy Statement as set forth under the caption "Election of Directors." Information relating to our executive officers is set forth in Part I of this Report under the caption "Executive Officers of Aastrom."

Information with respect to delinquent filings pursuant to Item 405 of Regulation S-K is incorporated by reference to the Proxy Statement as set forth under the caption "Section 16(a) Beneficial Ownership Reporting Compliance."

ITEM 11. EXECUTIVE COMPENSATION

The information relating to executive compensation is incorporated by reference to the Proxy Statement under the caption "Executive Compensation and Other Matters."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information relating to ownership of our equity securities by certain beneficial owners and management is incorporated by reference to the Proxy Statement as set forth under the caption "General Information—Stock Ownership of Certain Beneficial Owners and Management."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information relating to certain relationships and related transactions is incorporated by reference to the Proxy Statement under the captions "Certain Transactions" and "Compensation Committee Interlocks and Insider Participation."

PART IV

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

(a) The following documents are filed as part of this Report:

1. Financial Statements.

2. Financial Statement Schedule:

   All schedules are omitted because they are not applicable or not required, or because the required information is included in the Financial Statements or Notes thereto.

3. Exhibits:

   See Exhibit Index.

(b) Reports on Form 8-K:

No reports on Form 8-K were filed during the fourth quarter.

SIGNATURES

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

Date: September 14, 2001

AASTROM BIOSCIENCES, INC.

By: /S/ R. DOUGLAS ARMSTRONG, PH.D.

R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below on September 14, 2001 by the following persons in the capacities indicated.

Signature	Title
/S/ R. DOUGLAS ARMSTRONG, PH.D. **R. Douglas Armstrong, Ph.D.**	President, Chief Executive Officer and Director *(Principal Executive Officer)* *(Interim Principal Financial and Accounting Officer)*
/S/ FABRIZIO BONANNI **Fabrizio Bonanni**	Director
/S/ MARY L. CAMPBELL	Director

Mary L. Campbell	
/S/ ARTHUR F. STAUBITZ	Director
Arthur F. Staubitz	
/S/ JOSEPH A. TAYLOR	Director
Joseph A. Taylor	
/S/ ALAN M. WRIGHT	Director
Alan M. Wright	

EXHIBIT INDEX

Exhibit Number	Notes	Description of Document
3.1	A	Restated Articles of Incorporation of Aastrom.
3.2	B	Bylaws, as amended.
4.1	B	Specimen Common Stock Certificate.
4.2	B	Amended and Restated Investors' Rights Agreement, dated April 7, 1992.
10.1#	B	Form of Indemnification Agreement.
10.2#	B	Amended and Restated 1992 Incentive and Non-Qualified Stock Option Plan and forms of agreements thereunder.
10.3#	B	1996 Outside Directors Stock Option Plan and forms of agreements thereunder.
10.4#	B	1996 Employee Stock Purchase Plan and form of agreement thereunder.
10.7	B	Lease Agreement, dated May 18, 1992, between Domino's Farms Holdings, L.P. and Aastrom and amendments thereto dated February 26, 1993, October 3, 1994, November 16, 1994 and July 29, 1996.
10.8#	B	Promissory Note, dated November 18, 1993, for $120,000 loan by Aastrom to R. Douglas Armstrong, Ph.D. and amendment thereto dated October 30, 1996.
10.16	B	Collaborative Supply Agreement, dated December 16, 1996, between Aastrom and Anchor Advanced Products, Inc. Mid-State Plastics Division.
10.20#	B	Form of Employment Agreement.
10.21	B	License Agreement, dated July 17, 1992, between J.G. Cremonese and Aastrom and related addenda thereto dated July 14, 1992 and July 7, 1993.
10.22+	B	Collaborative Product Development Agreement, dated May 10, 1994, between SeaMED Corporation and Aastrom.
10.23+	B	Collaborative Product Development Agreement, dated November 8, 1994, between Ethox Corporation and Aastrom.
10.24+	B	License and Supply Agreement, dated April 1, 1996, between Immunex Corporation and Aastrom.
10.26	B	License Agreement, dated March 13, 1992, between Aastrom and the University of Michigan and amendments thereto dated March 13, 1992, October 8, 1993 and June 21, 1995.
10.27#	B	Employee Proprietary Information and Invention Agreement, effective June 1, 1991, between Aastrom and R. Douglas Armstrong, Ph.D.
10.29#	B	Employment Agreement, dated December 8, 1995, between Aastrom and Todd E. Simpson.
10.32#	B	Employment Agreement, dated October 26, 1995, between Aastrom and Alan K. Smith, Ph.D.
10.40	D	Amendment to License and Supply Agreement, dated August 25, 1997, between Immunex Corporation and Aastrom.
10.41+	C	Manufacturing Supply Agreement, dated as of August 14, 1998, by and between Aastrom and SeaMED Corporation.
10.42#	M	Employment Agreement, dated August 10, 1998, by and between Aastrom and Bruce Husel.

Exhibit Number	Notes	Description of Document
10.42#	C	Employment Agreement, dated August 10, 1998, by and between Aastrom and William Odell.

10.43	L	Strategic Planning Consulting Services and Collaboration Agreement, dated October 7, 1997, between Burrill & Company, LLC and Aastrom.
10.44		Not Used
10.45		Not Used
10.46#	N	Executive Retention and Severance Agreement, dated February 2, 1999, between Aastrom and R. Douglas Armstrong.
10.47		Not Used
10.48		Not Used
10.49#	H	Supplemental Agreement by and between Aastrom and Bruce W. Husel dated October 5, 1999.
10.50#	H	Supplemental Agreement by and between Aastrom and William L. Odell dated October 1, 1999.
10.51#	H	Supplemental Agreement by and between Aastrom and Todd E, Simpson dated September 24, 1999.
10.52		Not Used
10.53	H	Exclusive financial advisor agreement between Aastrom and Salomon Smith Barney Inc., dated September 10, 1999.
10.54#	I	Form of Supplemental Agreement to Employment Agreement between Douglas Smith and Aastrom.
10.55#	I	Pay to Stay Severance Agreement between R. Douglas Armstrong, Ph.D. and Aastrom dated October 15, 1999.
10.56#	I	Form of Pay to Stay Severance Agreement between Aastrom and Todd E. Simpson dated October 18, 1999, and between Aastrom and Alan Smith dated October 21, 1999.
10.57	J	Securities Purchase Agreement, dated February 28, 2000, by and between Aastrom and RGC International Investors, LDC (RGC).
10.58	J	Registration Rights Agreement dated February 28, 2000, by and between Aastrom and RGC.
10.59	J	Stock Purchase Warrant dated February 29, 2000.
10.60	K	Securities Purchase Agreement dated June 8, 2000, by and between Aastrom and RGC.
10.61	K	Registration Rights Agreement dated June 8, 2000, by and between Aastrom and RGC.
10.62	K	Stock Purchase Warrant dated June 8, 2000.
10.63#	O	Agreement Regarding Pay-to-Stay, by and between Aastrom and R. Douglas Armstrong, Ph.D. dated April 28, 2000.
10.64#	O	Agreement Regarding Pay-to-Stay, by and between Aastrom and Todd E. Simpson dated June 30, 2000.
10.65#	O	Agreement Regarding Pay-to-Stay, by and between Aastrom and Brian S. Hampson dated April 28, 2000.
10.66#	O	Form of Retention Bonus Agreement, by and between Aastrom and each of Brian S. Hampson, Bruce W. Husel and Todd E. Simpson.

Exhibit Number	Notes	Description of Document
10.67#	O	Form of Relocation Bonus Agreement, by and between Aastrom and each of Brian S. Hampson, Bruce W. Husel and Todd E. Simpson.
10.68#		Employment Agreement, dated October 24, 2000, by and between Aastrom and Audrey Hutter.
10.69#		Employment Agreement, dated February 1, 2001, by and between Aastrom and Steven Wolff.
23.1		Consent of Independent Accountants.

A Incorporated by reference to Aastrom's Quarterly Report on Form 10-Q for the quarter ended December 31, 1996, as filed on March 7, 1997.
B Incorporated by reference to Aastrom's Registration Statement on Form S-1 (No. 333-15415), declared effective on February 3, 1997.
C Incorporated by reference to Aastrom's Annual Report on Form 10-K for the year ended June 30, 1998, as filed on September 29, 1998.
D Incorporated by reference to Aastrom's Annual Report on Form 10-K for the year ended June 30, 1997, as filed on September 25, 1997.
E Incorporated by reference to Aastrom's Current Report on Form 8-K, as filed on July 15, 1998.
F Incorporated by reference to Aastrom's Current Report on Form 8-K, as filed on June 4, 1999.
G Incorporated by reference to Aastrom's Quarterly Report on Form 10-Q for the quarter ended December 31, 1998, as filed on February 11, 1999.
H Incorporated by reference to Aastrom's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999, as filed on November 12, 1999.

I Incorporated by reference to Aastrom's Quarterly Report on Form 10-Q for the quarter ended December 31, 1999, as filed on February 14, 2000.

J Incorporated by reference to Aastrom's Report on Form 8-K filed on March 3, 2000.

K Incorporated by reference to Aastrom's Registration Statement on Form S-3 (333-39698), as filed on June 20, 2000.

L Incorporated by reference to Aastrom's Registration Statement on Form S-1 (No. 333-37439), as filed on October 8, 1997.

M Incorporated by reference to Aastrom's Amendment to Registration Statement on Form S-1 (No. 333-37439), as filed on November 21, 1997.

N Incorporated by reference to Aastrom's Annual Report on Form 10-K for the year ended June 30, 1999, as filed on September 20, 1999.

O Incorporated by reference to Aastrom's Annual Report on Form 10-K for the year ended June 30, 2000, as filed on September 22, 2000.

+ Confidential treatment has been requested as to a portion of this exhibit.

Management contract or compensatory plan or arrangement covering executive officers or directors of Aastrom.

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of October 24, 2000, by and between Aastrom Biosciences, Inc., a Michigan corporation ("Employer") and Audrey Hutter ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. **Employment** Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. **Duties** Employee is engaged as Vice President Market Development. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. **Compensation**

3.1 ***Base Salary*** During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of One Hundred Sixty-five Thousand Dollars ($165,000), payable in semi-monthly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. **Term**

4.1 ***Commencement*** The employment relationship pursuant to this Agreement shall commence on January 2, 2001.

4.2 ***Termination at Will*** Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 ***Termination for Cause*** Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 ***Payment of Compensation Upon Termination*** Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. **Fringe Benefits**

5.1 ***Customary Fringe Benefits*** Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ***Accumulation*** Employee shall not earn and accumulate unused vacation in excess of twenty (20) days. Employee shall not earn and accumulate sick leave or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. **Invention, Trade Secrets and Confidentiality**

6.1 ***Definitions***

6.1.1 *Invention Defined.* As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 *Trade Secret Defined.* As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 ***Inventions***

6.2.1 *Disclosure.* Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 *Employer Property; Assignment.* Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the

patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 *Exclusion Notice.* The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 *Patents and Copyrights; Attorney-in Fact.* Both before and after termination of this Agreement (and with reasonable compensation paid by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 ***Trade Secrets***

6.3.1 *Acknowledgment of Proprietary Interest.* Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 *Covenant Not to Divulge Trade Secrets.* Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 *Confidential Information of Others.* Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 ***No Adverse Use*** Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 ***Return of Materials at Termination*** In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 ***Remedies Upon Breach*** In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute

proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. **Covenant Not to Compete** Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. **General Provisions**

8.1 ***Attorneys' Fees*** In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 ***Amendments*** No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ***Entire Agreement*** This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 ***Successors and Assigns*** The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 ***Waiver*** Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 ***Severable Provisions*** The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

8.7 ***Employment Eligibility*** During the term of this Agreement, Employee shall maintain citizenship in the United States or documentation to establish employment eligibility in compliance with the Federal Immigration Reform and Control Act of 1986.

9. **Employee's Representations** Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

Aastrom Biosciences, Inc.

By: /s/ R. Douglas Armstrong Ph.D.
R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer

EMPLOYEE:

/s/ Audrey Hutter
Audrey Hutter

Address: _____

_____

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of February 1, 2001, by and between Aastrom Biosciences, Inc., a Michigan corporation ("Employer") and Steven Wolff ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. **Employment** Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. **Duties** Employee is engaged as Vice President Medical Affairs. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. **Compensation**

3.1 ***Base Salary*** During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of Two Hundred Ten Thousand Dollars ($210,000), payable in semi-monthly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. **Term**

4.1 ***Commencement*** The employment relationship pursuant to this Agreement shall commence April 9, 2001.

4.2 ***Termination at Will*** Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 ***Termination for Cause*** Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 ***Payment of Compensation Upon Termination*** Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. **Fringe Benefits**

5.1 ***Customary Fringe Benefits*** Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ***Accumulation*** Employee shall not earn and accumulate unused vacation in excess of Fifteen (15) days. Employee shall not earn and accumulate sick leave or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. **Invention, Trade Secrets and Confidentiality**

6.1 ***Definitions***

6.1.1 *Invention Defined.* As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 *Trade Secret Defined.* As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 ***Inventions***

6.2.1 *Disclosure.* Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 *Employer Property; Assignment.* Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the

patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 *Exclusion Notice.* The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 *Patents and Copyrights; Attorney-in Fact.* Both before and after termination of this Agreement (and with reasonable compensation paid by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 ***Trade Secrets***

6.3.1 *Acknowledgment of Proprietary Interest.* Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 *Covenant Not to Divulge Trade Secrets.* Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 *Confidential Information of Others.* Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 ***No Adverse Use*** Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 ***Return of Materials at Termination*** In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 ***Remedies Upon Breach*** In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute

proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. **Covenant Not to Compete** Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. **General Provisions**

8.1 ***Attorneys' Fees*** In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 ***Amendments*** No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ***Entire Agreement*** This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 ***Successors and Assigns*** The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 ***Waiver*** Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 ***Severable Provisions*** The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

8.7 ***Employment Eligibility*** During the term of this Agreement, Employee shall maintain citizenship in the United States or documentation to establish employment eligibility in compliance with the Federal Immigration Reform and Control Act of 1986.

9. **Employee's Representations** Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

Aastrom Biosciences, Inc.

By: /s/ R. Douglas Armstrong Ph.D.
R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer

EMPLOYEE:

/s/ Steven Wolff
Steven Wolff

Address: _____

_____

Exhibit 23.1

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in each Registration Statement on Form S-8 (Nos. 333-51556, 333-38886 and 333-25021) and Form S-3 (Nos. 333-39698, 333-32914, 333-92675, 333-81399 and 333-60125) of Aastrom Biosciences, Inc. of our report dated August 10, 2001, except for Note 9, which is as of September 5, 2001 relating to the financial statements, which appears in this Form 10-K.

PricewaterhouseCoopers LLP

Minneapolis, Minnesota
September 11, 2001