BioSphere Medical

Delivering On The Promise Of Embolotherapy

2001 Annual Report

biosphere medical™

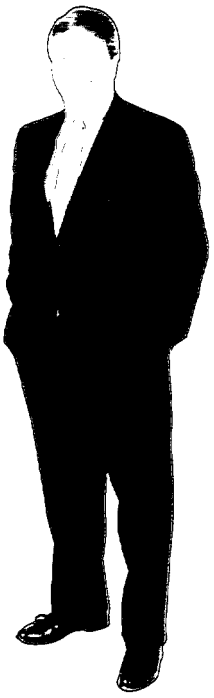
Innovating Embolotherapy

Embolotherapy, the minimally invasive treatment of hypervascularized tumors and vascular malformations by occluding their blood supply with small particles, is a rapidly emerging market. Our first major target is uterine fibroids, which afflict tens of millions of women worldwide. With the recently announced positive results from our Phase II pivotal clinical trial of Embosphere Microspheres for uterine fibroid embolization, we believe that we are well on the way to obtaining U.S. regulatory approval and one step closer to achieving our goal of becoming the world leader in products for the treatment of uterine fibroid embolization.

Important Note To Stockholders

Certain statements made in this Annual Report to Stockholders are forward-looking statements that are subject to risks and uncertainties. There are a number of important factors that could cause our future performance and results of operations to differ materially from such statements, including without limitation those set forth under the heading "Risk Factors that May Affect Future Operating Results" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2001, which is filed with the Securities and Exchange Commission.

Delivering On The Promise Of Embolotherapy

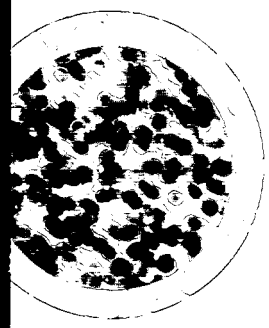


John M. Carnuccio, President and Chief Executive Officer

Dear Stockholder:

BioSphere Medical's primary mission is to become a global leader in the rapidly growing embolotherapy market. In embolotherapy, tiny particles are injected into blood vessels through a minimally invasive catheter to cut off the flow of blood to vascular malformations and benign and malignant tumors. Within this field, we are applying our proprietary technology to the large and growing uterine fibroid embolization (UFE) and liver cancer markets, which together represent a $600-$800 million opportunity worldwide.

I am pleased to say that in 2001 we made significant strides toward reaching our goal. In fact, the year was defined by a series of clinical advances and key business achievements. Among these, we made major progress in our UFE clinical trials in conjunction with driving demand for our lead product, Embosphere Microspheres (currently FDA approved for treatment of hypervascularized tumors and arteriovenous malformations), and introducing an improved new product– EmboGold Microspheres. As we further penetrated our target markets, we achieved record revenues, enhanced gross margins and significant growth in the number of embolization procedures performed during the year. We strengthened our corporate infrastructure by expanding our distribution network, substantially increasing our manufacturing capacity, broadening our management team and completing a follow-on public offering.



The Uterine Fibroid Embolization (UFE) Opportunity

Uterine fibroids are benign tumors which can cause symptoms such as excessive bleeding, pain and disfigurement. They afflict approximately 25 million women in the U.S. Industry sources indicate that 200,000 – 300,000 of the 600,000 hysterectomies performed in the U.S. each year are due to fibroids. Further, there is a large pool of approximately six million women domestically, who are symtomatic enough to see their doctor. Today, many of these women take drugs that are not curative and often have severe side effects such as permanent bone density loss, or they simply suffer silently.

To address this large market opportunity, BioSphere Medical became the first company to begin clinical testing under an FDA approved Investigational Device Exemption for UFE. UFE is a minimally invasive, catheter-based procedure in which tiny particles are injected into the blood vessels supplying the fibroids to occlude their blood supply, reduce their size and alleviate associated symptoms. We believe that many women will choose to have UFE procedures as they become more knowledgeable about the typical benefits, including the ability to leave the hospital in a day and resume normal activities in just five to seven days.

Favorable UFE Trial Results

One year follow-up results from our Phase I UFE clinical trial were reported at the January 2002 International Society For Endovascular Therapy meeting. According to Dr. James Spies, the lead investigator in this and our Phase II pivotal clinical trial, "Changes in bleeding, pain and overall quality of life were all highly significant at six months, and the fact that these improvements were maintained at one year is also a strong indication of durability." At the Society of Cardiovascular and Interventional Radiology meeting held in April of 2002, Dr. Spies reported similar results for up to six months of data from the Phase II pivotal clinical trial. Based on this favorable data, we plan to file a 510(k) during the second quarter of 2002 for FDA clearance of Embosphere Microspheres for UFE.

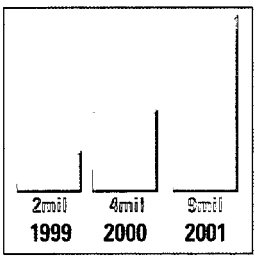
Milestones

The year 2001 was defined by a series of clinical advances and key business achievements

Pivotal UFE Clinical Trial Completed

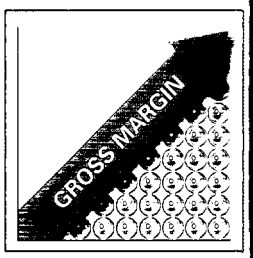
Positive Results From Phase II Pivotal Trial Reported April, 2002

Embolotherapy Revenues More Than Triple



Total Revenues Increase to $9 Million Revenues from Embolotherapy Products More Than Triple

Strong Gross Margins



Gross Margins Increase To Over 70%

Embolotherapy For New Markets

As we expand our proprietary technology to additional fast growing markets, we are focused on two major fields– liver cancer and neurological tumors. Millions of people have been infected by the Hepatitis B and Hepatitis C viruses, which can lead to liver cancer, the number one malignancy in the world. Today, primary liver cancer alone causes over 1.2 million deaths annually. We believe that, as therapeutic regimens are further defined, Targeted Liver Embolization (TLE) will become a significant market opportunity. Alone (bland embolization) or in conjunction with chemotherapeutic agents (chemo-embolization), our Embosphere Microspheres and EmboGold Microspheres are used to treat liver cancer.

We believe that the neurological market offers another high profile opportunity where we can leverage our product offering and improve patient care. Historically, embolotherapy has been used in various head and neck procedures as a means of blocking the blood supply to inoperable tumors or to minimize bleeding within targeted surgical areas. As applications within the brain are considered the most medically sensitive and complex, we believe the continued use of embolotherapy in these high-risk procedures attests to its overall efficacy and safety. We are currently developing distribution resources to bring our microsphere technology to the neurological field, where industry sources indicate the market potential could exceed $100 million.

Product Portfolio Expansion

In the third quarter, we achieved a major milestone with the launch of our premium product, EmboGold Microspheres. This product was developed based on feedback from interventional radiologists across the country who were already using our flagship Embosphere Microspheres, but were looking for improved procedural convenience. EmboGold Microspheres are supplied in a pre-filled syringe and are tinted to facilitate easier handling and procedural efficiency. Physician response has been positive, and we anticipate that EmboGold Microspheres will be an important part of our product mix in 2002 and beyond.

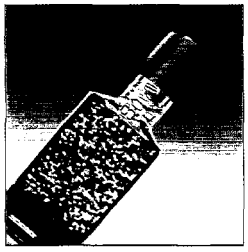
At the end of the year, we received regulatory clearance for our new EmboCath Hydrophilic Infusion Catheter, which we expect to launch commercially in the U.S. in the second half of 2002. This product is designed to take advantage of the unique features of our proprietary microsphere technology by providing interventional radiologists with a more efficient and cost effective method of delivering embolic material as well as diagnostic and therapeutic agents. This and other complementary products under development are being designed to allow us to capture more revenues from each embolotherapy procedure and further leverage our field sales organization.

Our HepaSphere SAP Microspheres are being used on an investigational basis in Japan to treat liver cancer. To date, over 100 primary liver cancer patients have been treated on an investigational basis in Japan; and we anticipate entering U.S. clinical trials in 2003. We also have other important early stage development programs for embolotherapy products. These products, including MR detectable microspheres, radiopaque microspheres, liquid embolics, drug delivery microspheres and others, are being designed to provide the physician with even more effective tools to relieve patient suffering.

Expanded Distribution

During the year, we expanded our U.S. distribution team exiting 2001 with a highly trained direct sales force dedicated to developing and expanding our interventional radiologist customer base.

EmboGold Microspheres Launched

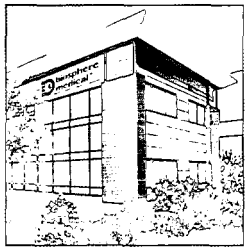


Premium Product Receives Strong Market Acceptance

Expanded U.S. Distribution

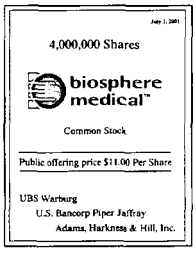
To Support Rapid U.S. Market Penetration

Expanded Manufacturing Capabilities



Capacity Increased To Accommodate Fourfold Increase In Microsphere Unit Sales

Successful Completion Of Public Offering



Company Nets Approximately $20 Million In New Capital and Expands Analyst Coverage

In January of this year, we announced the signing of an exclusive Pan European distribution agreement for our Embosphere Microspheres and EmboGold Microspheres with Terumo Europe. Terumo is a global medical technology company that develops, manufactures and markets a range of products and services, including market leading microcatheters and guidewires for most interventional procedures. This partnership is expected to positively increase recognition of our products as well as facilitate strong market acceptance within our target markets. Looking ahead, we plan to work with strategic partners to open new markets in Asia and Latin America.

Increased Manufacturing Capacity

In July, our new state-of-the-art manufacturing facility near Paris, France was completed. This facility provides us with the capability to accommodate up to a fourfold increase in unit demand for our microspheres.

Record Financial Performance

Continued strong demand for Embosphere Microspheres, coupled with the successful introduction of EmboGold Microspheres and the efforts of our sales team, allowed us to achieve record revenues of $9.0 million for the twelve months ended December 31, 2001- a 125% increase over revenues of $4.0 million in 2000 and in line with our expectations. Most importantly, our core embolotherapy revenues more than tripled to over $7 million. Our overall progress is also validated by the fact that new accounts and repeat orders, important indications of product acceptance, grew significantly during the year. Consolidated gross margin increased to 73% in 2001, compared with 63% in 2000. The net loss for fiscal 2001 was $10.3 million or $0.89 per share, compared with a net loss of $8.4 million or $0.87 per share in 2000. The increased net loss for the year was a reflection of our investment in an expanded sales force and research and development program as we drive the growth of our business.

In July, we successfully raised approximately $20 million in a follow-on public offering, providing the Company with sufficient capital for operations and expansion. In the fourth quarter of 2001, we acquired the remaining 15% ownership interest in Biosphere Medical SA (BMSA) France, giving us full control over manufacturing and distribution. We closed 2001 with cash and short-term investments totaling $23.1 million.

2002 - Moving Forward and Delivering on the Promise of Embolotherapy

For BioSphere Medical, 2001 was a year of substantial growth and progress on many fronts. We believe that our progress will continue in 2002 with increased revenues, new product launches, a UFE regulatory filing in the U.S. and possible approval, growth of our target markets, further strengthening of our distribution network and a drive toward our goal of profitability.

I want to thank our team of dedicated employees for their hard work; they are responsible for our continued success. I would also like to extend our gratitude to Jean-Marie Vogel, who stepped down as Chairman of the Board of Directors at the end of 2001. In this role, Jean-Marie provided valuable guidance and support to management, and we thank him for his contributions.

Thank you for your interest in BioSphere Medical. We appreciate the support and partnership of our stockholders, strategic partners and employees as we look forward to another year of continued progress.

John M. Carnuccio
President and Chief Executive Officer
April 15, 2002

Uterine Fibroid Embolization (UFE)

A Growing Market Worldwide

Uterine Fibroid Symptoms

Uterine fibroids are benign tumors whose symptoms can include any combination of severe bleeding, pain and disfigurement. Indeed, some women with large fibroids may appear to be pregnant. Untreated, the symptoms can persist until menopause, severely impacting the patient's quality of life.

Previous Treatment Options –
Invasive Surgery Or Drugs

In the United States, it is estimated that over five million women seek treatment annually for uterine fibroids. It is estimated that over 300,000 invasive surgical procedures, including 200,000 hysterectomies – surgical removal of the uterus – and 100,000 myomectomies – surgical removal of the fibroids – are performed in the United States each year because of fibroids. Each is a procedure that requires a hospital stay of 3–5 days and a recovery period of 6–8 weeks. Hormonal drugs are also used, but they do not offer a solution and can have severe side effects.

Due to the inadequacy of previous treatment options, millions of women have chosen to suffer silently.

Uterine Fibroid Embolization
The Minimally Invasive Alternative

In uterine fibroid embolization, a catheter is threaded through a very small hole in the leg to the uterine artery. Then our tiny, round Embosphere Microspheres or EmboGold Microspheres are injected into the artery. They travel to the blood vessels feeding the fibroid tumors and block their blood supply, causing them to shrink and die. The woman typically leaves the hospital within a day and is generally back to normal activities in 5–7 days.

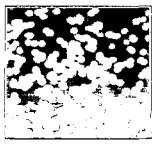
Positive UFE Clinical Trials

In December 2000, we initiated our pivotal Phase II clinical trial of Embosphere Microspheres for UFE under an investigational device exemption (IDE) granted by the FDA. Our six month follow-up data shows that 96 percent (80 of 83) of the women stated that they would recommend UFE to a friend. Clinical indices, such as reduction of pelvic pain and discomfort, were likewise positive at the six month follow-up. Two independent studies presented at the Society of Cardiovascular and Interventional Radiology meeting held in April, 2002 showed that well over 90 percent of UFE patients were satisfied with their results.

Products for Embolotherapy Procedures

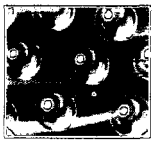
Our objective is to become the premier embolotherapy company in the world. To that end, we are developing a family of products for embolotherapy. Three of our products have been cleared by the FDA for marketing in the United States – Embosphere Microspheres, EmboGold Microspheres and the EmboCath Hydrophilic Infusion Catheter. In addition, Embosphere Microspheres and EmboGold Microspheres are on the market in the European Union and Canada; and Embosphere Microspheres are on the market in Australia. A fourth product – the EmboWire Hydrophilic Guidewire – is, we believe, in the final stages of regulatory clearance.

Embosphere Microspheres



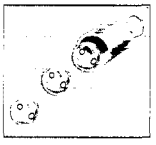
Embosphere Microspheres was our first product and has been used in thousands of cases worldwide to treat uterine fibroids, liver cancer, neurovascular disorders and other conditions.

EmboGold Microspheres



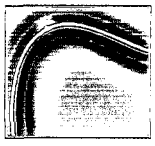
Building upon our proven Embosphere Microspheres technology, we launched our visible EmboGold Microspheres during the third quarter of 2001. This product has gained market share very rapidly, and we anticipate continued success in 2002.

EmboCath Hydrophilic Infusion Catheter



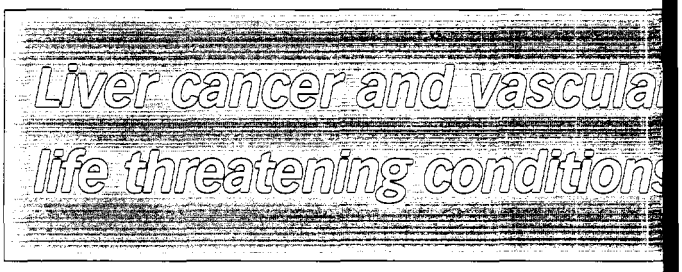
Developed for the infusion of embolics as well as diagnostic and therapeutic agents, we are confident that the EmboCath Hydrophilic Infusion Catheter will gain rapid acceptance as we introduce it to the market later this year.

EmboWire Hydrophilic Guidewire



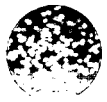
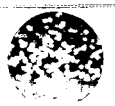
Virtually all catheter-based procedures utilize a guidewire. The EmboWire Hydrophilic Guidewire is designed for use in peripheral interventional procedures including embolotherapy. We anticipate a launch later in 2002 for this exciting new product.

We believe that the potential applications of embolotherapy are bound only by the ingenuity of physicians and the companies that support them. We intend to continue being the company with the most innovative embolotherapy products used to treat conditions that afflict millions.



malformations in the brain are just two of the
hat are treated using embolotherapy.

Embolotherapy Product Summary

	Research	Pre-clinical	Clinical Trials/ Market Evaluation	Received U.S. Regulatory Approval
Embosphere Microspheres for General Embolization*				
Embosphere Microspheres for Uterine Fibroid Embolization*				
EmboGold Microspheres**				
EmboCath Hydrophilic Infusion Catheter				
EmboWire Hydrophilic Guidewire				
HepaSphere SAP Microspheres				
Larger Size Microspheres				
Gelatin Free Microspheres				
More Elastic Microspheres				
Sensor Catheter				
MR Detectable Microspheres				
Radiosphere Microspheres				
TempRX Temporary Microspheres				
LiquiDx Liquid Embolic				
ViaSphere Drug Delivery Microspheres				

* Also cleared for use in general embolotherapy procedures, including uterine fibroid embolization, in the European Union, Canada and Australia.
** Also cleared for use in general embolotherapy procedures, including uterine fibroid embolization, in the European Union and Canada.

UNITED STATES
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: December 31, 2001

or

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

For the transition period from to

Commission File Number: 0-23678

BioSphere Medical, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**04-3216867**
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification No.)

1050 Hingham St., Rockland, Massachusetts 02370
(Address of Principal Executive Offices) (Zip Code)

(781) 681-7900
(Registrant's telephone number, including area code)

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

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $.01 par value
(Title of class)

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

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

The aggregate market value of voting Common Stock held by non-affiliates of the registrant was $76,630,000 based on the closing price of the shares as reported by the Nasdaq National Market on March 16, 2002.

Number of shares outstanding of the registrant's Common Stock as of March 16, 2002 was 12,910,495.

Documents incorporated by reference:
Proxy Statement for the 2002 Annual Meeting of Stockholders—Part III.

PART I

Item 1. BUSINESS

We are pioneering the use of our proprietary bio-engineered acrylic beads, known as microspheres, for medical applications using embolotherapy techniques and also to develop potential applications in several non-embolotherapy applications. We believe microsphere technologies, such as our proprietary microsphere platform, are enabling the rapid development of a new, "micro-interventional" market. We expect that micro-interventional devices will expand the capability of catheter–based interventional technologies and permit clinicians to treat medical conditions in a more effective and minimally invasive manner.

Embolotherapy is a minimally invasive procedure in which embolic materials, such as our microspheres, are delivered through a catheter into the blood vessels to inhibit blood flow to tumors or vascular defects or to control blood loss presurgically. Our initial product, Embosphere® Microspheres, is targeted for treatment of hypervascularized tumors and arteriovenous malformations. Hypervascularized tumors are tumors that have a large number of blood vessels feeding them and include certain tumors affecting the brain and spinal cord, tumors in the uterus, known as uterine fibroids, and tumors associated with primary liver cancer. By selectively blocking the tumor's blood supply, embolotherapy is designed to cause the tumor to shrink and necrose. Based on preliminary research, we believe that our microsphere technology platform can also be adapted to deliver drugs, living tissue or genetic material to targeted sites.

Our microspheres have a variety of characteristics that we believe make them preferable to other embolic materials currently used in embolotherapy. Specifically, we have designed our products to be easier to use and their delivery to the tumor more targeted and controlled, which we believe will result in better outcomes for the patient. By improving the practice and awareness of embolotherapy and the benefits of our products, we believe that patients who are currently untreated, surgical candidates and patients considering treatment with other embolics may seek treatment with our microsphere technology.

We believe that our platform microsphere technology also has several non-embolotherapy applications, such as tissue bulking, repair and regeneration. In this context, we are exploring and/or developing microspheres for use in the treatment of a number of conditions, including stress urinary incontinence and gastroesophageal reflux disease.

BioSphere Medical, Inc. was originally incorporated as a Delaware corporation in 1993 under the name BioSepra Inc., as a chromatography media company. During 1999, we strategically refocused our business on the development and commercialization of our proprietary microspheres for medical applications. During 2000, we established two wholly owned subsidiaries to pursue the development of our microsphere technologies in applications outside of, and complementary to, embolotherapy. In May 2000, we established Biosphere Medical Japan, Inc., a Delaware corporation, to develop and commercialize Embosphere Microspheres and HepaSphere SAP™ Microspheres in the Far East. In December 2000, we established BSMD Ventures, Inc., also a Delaware corporation, to explore and develop non-embolotherapy applications for our proprietary microspheres.

INDUSTRY OVERVIEW

Embolotherapy Markets

Embolotherapy has been in use for more than 20 years by interventional radiologists to mechanically block the flow of blood to treat certain peripheral tumors and arteriovenous malformations and to control blood loss. Historically, embolotherapy has been used in various brain-based procedures as a means of blocking the blood supply to inoperable tumors or to minimize bleeding within targeted surgical areas. As applications within the brain are considered among the most medically sensitive and complex, we believe the continued use of embolotherapy in these high-risk procedures attests to its overall safety and efficacy. In recent years, interventional radiologists in the United States, Europe and Japan have begun to expand the scope of

embolotherapy to include uterine artery embolization and the treatment of certain cancers, including liver cancer. Moreover, a growing number of affected people are taking proactive steps in seeking alternative treatments, particularly as a result of increased general awareness brought about by the proliferation of medical internet sites.

We refer to the use of embolotherapy as a method of blocking blood flow to tumors and other malformations as passive embolotherapy. We believe the potential market for passive embolotherapy continues to expand beyond niche neurovascular applications into broader medical opportunities, such as uterine fibroid and liver tumor embolization.

In addition, in a process we refer to as active embolotherapy, we are pursuing the development of microspheres as well as other technologies designed to release embedded drugs, live cells, ionizing radiation or genetic material specifically at a targeted site. We believe that delivering a drug directly to the tumor site and then releasing it over time may increase the effectiveness of the drug while decreasing the adverse side effects.

Uterine Fibroids

Uterine fibroids are non-cancerous tumors growing within or on the wall of the uterus. Their cause is unknown. Most patients with uterine fibroids do not initially have symptoms and remain untreated until the patient experiences abnormal bleeding, increased urinary frequency, pain, swelling or fertility difficulties.

Until now, women suffering from uterine fibroids have had few treatment options. These existing treatment options include the following:

- **Hysterectomy.** Hysterectomy is a surgical procedure to remove the uterus. While hysterectomy has a relatively low complication rate, it requires a hospital stay of several days, a recovery period of up to six to eight weeks and results in loss of fertility for women of child-bearing age. Furthermore, hysterectomies have been tied to adverse psychological effects, as well as the onset of early menopause.
- **Myomectomy.** Myomectomy is the surgical removal of the uterine fibroids without removal of the uterus. It is usually performed on women who wish to preserve their fertility. In addition to the invasiveness of the procedure, the most significant disadvantage of myomectomy is a 10 to 30 percent recurrence rate. Even though a myomectomy has been the only procedure available to women with severe symptoms from uterine fibroids that wish to preserve fertility, the recurrence rate and invasiveness have resulted in resistance from both third party payors and patients. Relatively few myomectomies are performed in relation to the number of eligible patients.
- **Medical Management and "Watchful Waiting."** About 95 percent of symptomatic fibroid patients either receive hormone treatment on a temporary basis to relieve symptoms or remain untreated and tolerate the symptoms. Even if the patient receives treatment, once treatment ceases, the uterine fibroids usually regrow. While hormone treatment temporarily reduces symptoms, patients often experience side effects associated with the accompanying hormonal changes. Moreover, women cannot conceive while taking the hormones. Women with less severe symptoms who are, therefore, not candidates for hormone treatment, and those seeking to conceive have few satisfactory options. In these circumstances, physicians usually monitor symptoms and will administer therapy only if the condition worsens.

The therapies currently available for treating uterine fibroids may have significant drawbacks including:

- temporary or permanent loss of fertility for women of child-bearing age;
- lengthy recovery periods;
- premature menopause and related symptoms;
- high costs, including costs of medications, surgical procedures, and frequent and long hospital stays;

- discomfort and side effects from invasive surgical procedures and hormone therapy; and
- risk of recurrence of the fibroids.

Another method of treating uterine fibroids, more recently adopted by physicians, is uterine artery embolization. Though not approved by the FDA for this specific use, another embolic material commonly used today in uterine artery embolization is polyvinyl alcohol, or PVA. Polyvinyl alcohol has several limitations, including:

- **Inconvenience and limited effectiveness.** Polyvinyl alcohol often clogs in the catheter, interrupting the procedure and necessitating potentially hazardous, costly and time-consuming catheter replacement. In addition, because of its imprecise size and shape, polyvinyl alcohol may not fully occlude the blood vessel, allowing the blood to circumvent the embolic material and continue to feed the tumor.
- **Limited control.** Polyvinyl alcohol often fragments and aggregates, or clumps, in the blood vessel, causing vessel blockages prior to reaching the desired site of blood flow occlusion. In addition to catheter problems, clumping during embolization is clinically problematic. If clumping occurs at non-targeted sites in the vessel after injection into the artery, incomplete embolization can occur. In addition, occlusions can block desired normal blood supply causing undesired necrosis or death of healthy tissue.
- **Chronic inflammatory response.** Polyvinyl alcohol often stimulates an inflammatory response by the body that persists for an extended period of time.

Based upon the shortcomings in existing technologies and therapies we discussed above, we believe there are significant opportunities in developing and commercializing alternative embolic treatment products for patients suffering from uterine fibroids. For example, there are approximately 300,000 hysterectomies performed annually in the United States for uterine fibroids. We believe that substantially all of these cases could be effectively treated with our Embosphere Microspheres.

Primary Liver Cancer

Primary liver cancer originates in the liver, rather than traveling to the liver from another cancer site in the body. Over 70 percent of primary liver cancers are inoperable and are, therefore, treated primarily with chemotherapy or radiation. However, due to the destructive nature of both radiation and chemotherapy, these therapies have traditionally been associated with the following limitations and side effects:

- **Radiation.** While radiation therapy can shrink or eliminate certain individual tumors, its use in treating liver cancer is limited. Since it is difficult to isolate radiation exposure to the liver tumor, radiation therapy often results in damage to the surrounding non–tumorous tissue.
- **Chemotherapy.** Chemotherapy seeks to control cancer by selectively killing the more-rapidly-dividing cancer cells and is widely used for treating cancer elsewhere in the body. The use of systemically delivered chemotherapy agents, however, has shown little benefit in treating liver cancer. Similar to the limitations of radiation therapy, therapeutic doses of chemotherapy to the cancerous tissue have a damaging effect on the normal surrounding tissue.

Other treatments currently under investigation to treat inoperable primary liver cancer are radio frequency tumor ablation, which seeks to kill the tumor by means of destructive electrical energy, and embolization. Interventional radiologists are also currently using chemoembolotherapy to treat liver cancer. Chemoembolotherapy refers to the delivery of drugs in a mixture that contains embolic materials to create a higher localized concentration of the drug.

We believe there are significant opportunities in developing and commercializing alternative embolic products for use in non-operable liver cancer cases.

Non-Embolotherapy Applications

Advances in cell biology are resulting in rapid advances in the fields of organ and tissue repair, reconstruction and regeneration, which we generally refer to as tissue engineering. These developments in tissue engineering are targeted at facilitating the body to heal itself through the delivery of molecular signals, cells or supporting structures to the appropriate sites in the body.

In certain conditions, including stress urinary incontinence, gastroesophageal reflux disease, urinary reflux in infants and certain skin conditions, the normal anatomic supports are not present in the body. Injecting fillers into the existing structures to bulk them up, referred to as tissue bulking, is designed to recreate the missing anatomic supports, thereby eliminating the condition.

Tissue repair and regeneration involves the development of bioartifical cells, tissues and supporting matrixes, which are scaffolds that hold the cells or tissues together. These tissue scaffolds may also be developed from synthetic polymers. Tissue scaffold products have a number of potential applications, including cartilage and bone repair as well as organ supplements or replacements.

OUR BUSINESS STRATEGY

Utilizing our platform microsphere technology, our strategy is to develop and commercialize innovative embolotherapy products for conditions where minimally invasive treatments do not currently exist. Because our primary focus is on embolotherapy, our strategy, with respect to other business opportunities, is to develop these products through proof of principle and then seek strategic partnerships to complete the commercialization process. Our criterion for product selection is that the product must have the potential to become the global leader in a significant market. The key elements of our strategy are as follows:

- **Continue to advance our microsphere technology for use in current passive embolotherapy applications.** We are focusing the initial implementation of our microsphere technology on addressing large embolotherapy market opportunities. We believe that embolotherapy will represent an attractive alternative to the current treatment options, many of which are invasive surgical procedures or have other significant drawbacks. We received FDA clearance in April 2000 for use of Embosphere Microspheres in the embolization of arteriovenous malformations and hypervascularized tumors in the United States. We intend, pending FDA clearance or approval, to market our products for use in embolization of uterine fibroids. We have recently completed the enrollment of our pivotal Phase II clinical trial to support an application for marketing clearance or approval from the FDA for the use of our Embosphere Microspheres in the specific treatment of uterine fibroids. Our Embosphere Microspheres are also approved in the European Union, Australia and Canada. In Japan, our Hepasphere SAP Microspheres have been used experimentally in over 100 patients for liver cancer embolotherapy.

- **Develop new embolotherapy platforms, including active microsphere technologies that advance the scope of embolotherapy into new therapeutic applications.** We believe that there are opportunities to use microspheres as well as other technologies to advance the scope of embolotherapy into new therapeutic applications. We are currently pursuing opportunities in the area of active embolotherapy, which is the use of embolotherapy to deliver therapeutic agents directly to a target site. Therapeutic agents may include drugs, ionizing radiation, live cells or genetic material. We believe that active embolotherapy could, for example, allow blocking of the blood flow to the tumor site while allowing targeted, more effective delivery of therapeutic agents. We are currently conducting pre-clinical research on our Viasphere™ Microspheres, which are being designed as precisely-sized highly hydrophilic microspheres to which living cells, genetic materials or drugs are attached. We are also conducting pre-clinical research on our Radiosphere™ Microspheres which are similarly designed to deliver targeted radiation therapy.

- **Pursue opportunities for microsphere technology in other medical applications with large target markets and commercialize these opportunities primarily through strategic alliances and partnerships.** We believe that there are significant opportunities for applying our platform microsphere technology beyond embolotherapy. These opportunities include configuring our microspheres to serve as a bulking agent to treat stress urinary incontinence, gastroesophageal reflux disease and dermal repair, or as a tissue scaffold for tissue or organ regeneration. We believe that our microspheres will be an attractive treatment alternative in each of these markets. We intend to establish strategic alliances or partnerships as the primary vehicle to commercialize products outside the field of embolotherapy based on our microspheres.

- **Build a broad, value-added ancillary product portfolio to facilitate embolotherapy procedures.** We intend to complement our microsphere product line by offering value-added ancillary products used in each procedure, such as specialty catheters, guidewires and other delivery systems. Our ancillary products will be specifically designed for our targeted procedures and will be aimed at facilitating ease of use, enhancing clinical performance during the procedure and providing differentiating benefit to our customers. We believe that this will enable us to leverage our existing distribution channels and satisfy more of our physician customer's needs by providing more complete product solutions for each procedure.

- **Build a sales infrastructure consistent with the customer base and the geographic distribution of the patient population.** We intend to market our products primarily through direct sales efforts in the United States and through a combination of distributors, field representatives and direct marketing support in other parts of the world. In the United States, there are approximately 2,500 to 3,000 interventional radiologists and 200 to 300 interventional neuroradiologists. We believe that we can market effectively to these groups with a relatively small, targeted sales force. We intend to tailor our sales infrastructure to the demographics of the patient population for each of the targeted markets. For example, there are a large number of primary liver cancer patients in Asia due to the prevalence of hepatitis. Accordingly, we will likely choose to focus more of our sales resources in Asia on our Hepasphere SAP Microspheres product than on our Embosphere Microspheres.

PRODUCTS

Our innovative microsphere technology evolved out of approximately 15 years of research and development of polymer formulations used in the field of biological separations and drug purification. In 1999, we made a strategic decision to focus on microsphere technologies for medical applications. We believe that our microsphere technology is a platform technology which can be configured in several different ways to have applications as a pure embolic material, an embolic material linked to a gene or drug, a bulking agent or a scaffold for tissue engineering.

The following table summarizes information about our principal products and products under research and development.

PRODUCT / PRODUCT CANDIDATES	POTENTIAL MARKETS	STATUS	TARGET CUSTOMERS
EMBOLOTHERAPY			
Embosphere® Microspheres	Hypervascularized tumors, arteriovenous malformations	Marketed in United States, Canada, Australia and European Union	Interventional Radiologist; Interventional Neuroradiologist
	Uterine fibroids	Marketed in Canada, Australia and European Union Pivotal Phase II clinical trial in United States	Interventional Radiologist
EmboGold™ Microspheres	Hypervascularized tumors, arteriovenous malformations	Marketed in United States, Canada, Australia and European Union	Interventional Radiologist; Interventional Neuroradiologist
	Uterine fibroids	Marketed in European Union, Canada and Australia Pivotal Phase II clinical trial in United States	Interventional Radiologist
Hepasphere SAP™ Microspheres	Liver cancer	Investigational use in human patients in Japan	Interventional Radiologist
TempRx™ Microspheres	Trauma, hemorrhage	Research	Interventional Radiologist
LiquiDx™ Microspheres	Abdominal aortic aneurysm graft leaks	Research	Interventional Radiologist
	Cerebral aneurysm	Research	Interventional Neuroradiologist
Radiosphere™ Microspheres	Cancer	Research	Interventional Radiologist
Viasphere™ Microspheres	Cancer	Research	Interventional Radiologist
TISSUE ENGINEERING			
MatrX™ Microspheres	Urinary incontinence	Pre-clinical	Urologist
	Vesicoureteral reflux	Pre-clinical	Urologist
	Facial contour defects	Pre-clinical	Dermatologist
	Gastroesophageal reflux disease	Research	Gastroenterologist
GenS2™ Microspheres	Tissue regeneration	Research	Orthopedic Surgeon Dermatologist

PASSIVE EMBOLOTHERAPY

Embosphere Microspheres

Our initial product, Embosphere Microspheres, is intended for use in passive embolotherapy to block the blood supply to hypervascularized tumors and arteriovenous malformations. Embosphere Microspheres have been used in Europe, the United States, Canada and Australia to treat hypervascularized tumors and arteriovenous malformations and to presurgically control blood loss. We believe that if we receive clearance or approval from the FDA specifically for uterine artery embolization, the principal application of the Embosphere Microspheres will be for this indication.

Uterine artery embolization is a minimally invasive procedure performed by interventional radiologists. In this procedure, microspheres are injected through a small catheter into the blood vessels feeding the fibroid tumor, preferentially blocking the blood supply to the fibroids, but not to the surrounding healthy tissues. The goal of the uterine artery embolization procedure is to eliminate the flow of blood to the uterine fibroid, thereby alleviating related symptoms, while preserving normal uterine and ovarian function.

We believe that embolotherapy is a significantly more attractive alternative in the treatment of uterine fibroids, particularly when compared to the invasiveness of such surgical procedures as hysterectomy or myomectomy, or even when compared to hormone therapy and "watchful waiting." Current therapies can have significant adverse side effects including temporary or permanent loss of fertility, lengthy recovery periods, high costs, discomfort and risk of recurrence of fibroids.

Although the effect of uterine artery embolization on continued fertility has not been established, we believe that uterine artery embolization has the potential to preserve the fertility of the patient that would otherwise be lost through hysterectomy or may be compromised by the use of current therapies or technologies, and to reduce or eliminate the risk of recurrence of the uterine fibroid tumor and the complications associated with myomectomy. Most uterine artery embolization procedures can be performed in less than one hour, while the patient is sedated, but awake. The patient generally stays overnight in the hospital to manage any discomfort associated with the procedure and typically returns to everyday activities in three to five days. In contrast, hysterectomy patients undergo general anesthesia, stay in the hospital for four to five days and have a recovery period lasting up to six to eight weeks.

Embolotherapy using polyvinyl alcohol has several limitations associated with its imprecise size and shape, including less effective occlusion of the blood supply to the tumor, inflammation and untargeted embolization resulting in the injury of the surrounding normal tissue. Independent studies have indicated that Embosphere Microspheres have a variety of characteristics that may make them preferable to polyvinyl alcohol. These include:

- **Uniform Spherical Shape/Calibrated Particle Size.** We are able to synthesize beads with uniform sizing and a spherical shape. When embolic materials are irregularly shaped or sized, as is the case with polyvinyl alcohol, clinicians find vessel targeting more difficult, and may also experience an increased incidence in unwanted embolization of blood vessels away from the site of the tumor.
- **Compliant and Resilient Properties.** We have developed a soft, elastic microsphere, that has the capability to compress significantly. Consequently, clinicians can deliver these beads through microcatheters. Many clinicians prefer using microcatheters during embolization since such catheters minimize the frequency of artery or vessel spasm during the procedure. Vessel spasm can be of particular concern during uterine artery embolization as it can disrupt the flow of blood. Clinicians rely on blood flow during embolization to direct the microspheres to the vessel targeted for occlusion.
- **Hydrophilic Properties.** As a result of the materials used to manufacture microspheres, our products are hydrophilic, which means that they absorb moisture. This characteristic is important in that it prevents the microspheres from clumping in the catheter and the artery during the procedure.

- **Non-biodegradability.** Our microspheres are composed of a synthetic three-component polymer that is compatible with the human body. This polymer is insoluble and non-biodegradable. We believe, therefore, that our Embosphere Microspheres are an appropriate agent for permanent vessel occlusion.
- **Cell Adhesion.** Our Embosphere Microspheres are cross-linked with a cell adhesion promoter composed of gelatin. This material promotes cell adhesion, resulting in a more rapid, stable and complete occlusion of the vessel.
- **Charged Surface Property.** Our microspheres are positively charged, enabling them to attach to the negatively-charged blood vessel wall. This attachment to the vessel wall minimizes the potential for the microspheres to migrate to non-targeted vessels.

Embosphere Microspheres are currently available in six sizes, from 40 to 1,200 microns, based on current customer requirements and targeted applications. They are designed to precisely fit the blood vessels, resulting in targeted and controlled occlusion. They can be used with existing, commercially available catheters and delivery systems. We anticipate that subsequent generations of Embosphere Microspheres, such as our EmboGold™ Microspheres, will incorporate new product characteristics. These new product characteristics may include improved cell adhesion properties and an improved ability for the physician to visualize the product using conventional x-ray or magnetic resonance imaging during administration. All of these products may require a new 510(k) approval. In February 2002, we began selling EmboSphere Microspheres in a new enhanced vial package.

We received CE Mark approval of our Embosphere Microspheres in the European Union in 1997 and more recently received marketing approval in Australia and Canada. In April 2000, we received marketing clearance from the FDA for our Embosphere Microspheres, through a 510(k) notification for hypervascularized tumors and arteriovenous malformations.

The 510(k) clearance for hypervascularized tumors and arteriovenous malformations does not specifically cover treating uterine fibroids. For the treatment of uterine fibroids through embolization, we recently completed enrollment of a clinical trial under an investigation device exemption to support an application for clearance or approval from the FDA for this specific indication. In January 2000, we initiated a Phase I clinical trial of Embosphere Microspheres for uterine artery embolization. Thirty patients were enrolled in the multi-center study at Roxborough Memorial Hospital, Philadelphia, the Miami Cardiac and Vascular Institute, Miami and Georgetown University Medical Center, Washington, D.C., as of June 2000. These patients were followed for a period of one year in accordance with the study plan. In October 2000, we initiated our pivotal Phase II clinical trial of the safety and efficacy of Embosphere Microspheres for uterine artery embolization, in which we studied an expanded patient population of 100 patients at seven clinical sites. These sites included Miami Cardiac and Vascular Institute, Miami; Roxborough Memorial Hospital, Philadelphia; Piedmont Hospital, Atlanta; Georgetown University Medical Center, Washington D.C.; Women's Health Center, Phoenix; Albany Medical Center, Albany; and Beverly Hills Center for Special Surgery, Beverly Hills. We announced full enrollment of the UAE arm of this study in September 2001 and, in January 2002, announced full enrollment of the remaining hysterectomy study arm.

EmboGold™ Microspheres

EmboGold Microspheres, an enhanced version of Embosphere Microspheres, were launched in the US in September 2001 after receiving FDA clearance earlier in the year. In March 2002, we received CE Mark approval in the European Union. This product enhancement added color to the spheres for improved visibility during preparation and injection. EmboGold Microspheres are provided in a special 20cc syringe and packaged in a sterile Tyvek® sealed tray. The syringe container was designed to provide added convenience in handling and preparation.

Hepasphere SAP™ Microspheres

Through our wholly owned subsidiary, Biosphere Medical Japan, Inc., we are developing Hepasphere SAP Microspheres for the treatment of primary liver cancer. Our Hepasphere SAP Microspheres are expandable microspheres for injection via catheter into the blood vessels feeding the liver cancer tumor. Once at the tumor

site, they are designed to expand by absorbing water from the blood and effectively block the blood supply to the tumor. Targeted liver embolotherapy is intended to starve the liver tumor, without damaging the surrounding tissues or causing any adverse side effects on other parts of the body, such as those associated with chemotherapy and radiation.

Over 100 primary liver cancer patients have been treated to date with Hepasphere SAP Microspheres on an investigational basis in Japan. In September 1999, we obtained a worldwide exclusive license to Hepasphere SAP Microspheres from its Japanese inventor. We plan to apply to the Japanese Ministry of Health and Welfare for marketing approval within the next 18 to 24 months.

TempRx™ Microspheres

We believe that a significant opportunity exists for temporary or resorbing embolic materials. Currently, embolic materials are frequently used to temporarily treat internal bleeding from trauma or specific disease and we believe that this could be a suitable application for temporary embolics. We believe that there is also a growing interest to use temporary or dissolving embolics in many current embolization applications, including liver and fibroid embolization. We are currently conducting research on our TempRx Microspheres as temporary embolics.

LiquiDx™ Microspheres

We are in the research stage of developing liquid embolics, or embolics that are in a liquid state when injected and, depending on the application, subsequently convert to a solid gel. Potential applications include treatment of endovascular graft leaks, aneurisms, and large vessel embolization applications including pelvic congestion syndrome and varicocele.

ACTIVE EMBOLOTHERAPY

We believe that our microspheres which are being designed to deliver drugs, radioactive material or genetic materials may have several advantages over current gene therapy, drug delivery or radiation products, including the direct delivery to tumor. Our microspheres for active embolotherapy will be designed to deliver the drug or gene therapy product directly to the tumor, avoiding the potential side effects associated with high levels of circulating drugs, genes, or radiation after an intravenous infusion through the blood vessel system. Direct delivery should permit the use of higher, potentially more effective, dosage of the product.

Radiosphere™ Microspheres

We believe the first step in marketing embolics that can deliver drugs or agents to treat cancer will be to develop microspheres that are "loaded" with drugs or agents at the treatment center using currently available equipment and techniques. We are developing our microsphere technology platform to be specifically formulated to express a high affinity for certain radioactive compounds. We believe that these spheres, when loaded, can be injected through a catheter to deliver radiation treatment directly to the tumor site. We believe that transvascular targeting of radiation is a potentially superior method to currently existing radiation treatment modalities because it offers a conceptually optimum way of uniformly dosing the tissue that is most actively proliferating while, at the same time, minimizing dosage to non-targeted areas. We also believe this approach will simplify logistical and handling requirements for radioactive materials in a hospital setting such as storage and shelf life. We have completed proof of concept for this technology and we expect to initiate pre-clinical testing in early 2003.

Viasphere™ Microspheres

We are conducting early-stage research on our Viasphere Microspheres, which are being designed as precisely-sized highly hydrophilic microspheres to which genetic materials or drugs are attached. We are developing these microspheres to be injected into the blood vessels feeding the tumor. We expect that once the flow of blood to the tumor has been occluded, Viasphere Microspheres will begin delivering concentrated genes or drugs into the tumor.

Other Embolization Products

We intend to develop and commercialize other embolization products that include:

- delivery systems for embolic materials, such as specialty catheters and guidewires,
- procedure-enhancing technologies that are designed to improve the uniformity of microsphere dispersion during injection, reduce radiation exposure and optimize efficiency of procedure time and implanted material, and
- additional embolic materials such as innovative coils, embolics that solidify upon injection and resorbable embolics to treat aneurisms and large arteriovenous malformations, as well as for specific tumors based upon their type or location.

In November 2001, we announced that we had received FDA clearance to market our EmboCath™ Infusion Catheter. The EmboCath Infusion Catheter is a micro-catheter style catheter that is designed to be used to inject embolization material in the pelvic and abdominal region and has properties that we believe optimize the unique design of our hydrophilic and compressible microspheres.

NON-EMBOLOTHERAPY TECHNOLOGIES

MatrX™ Microspheres

Our MatrX Microspheres product, currently in pre-clinical development, are highly hydrophilic synthetic microspheres designed to cause tissue bulking as a means to provide anatomic support in disease conditions where this support is missing. MatrX Microspheres preparations will be designed to be easily injectable yet large enough to avoid digestion within the body. We anticipate that the microsphere matrix, once injected, will be rapidly populated by surrounding cells and provide a stable, mechanically resistant tissue bulking structure. Potential applications of MatrX Microspheres preparations for tissue bulking include:

- **Stress Urinary Incontinence.** Approximately four million adults in the United States suffer from stress urinary incontinence, which is the involuntary loss of urine during coughing, laughing, sneezing, jogging, or any other activity which causes a sufficient increase in pressure within the abdomen. Stress urinary incontinence is currently treated in a variety of ways, but the majority of patients are managed with techniques that treat the symptoms, but do not restore urinary continence. Most curative approaches to the treatment of urinary incontinence require significant surgical interventions.

  Tissue bulking agents are either biologically derived or synthetic and are designed to be injected in or near the bladder neck to increase tissue bulk. While bulking procedures are gaining acceptance, the body typically absorbs biologically-derived bulking agents, requiring retreatment. Other limitations include migration of the synthetic agents to other non-affected parts of the body causing adverse health effects, incompatibility of the synthetic agents with the human body and difficulty in injecting the agents into the walls of the urethra. Accordingly, currently available therapies provide only limited benefit in the treatment of stress urinary incontinence.

  We are currently developing our MatrX Microspheres tissue-bulking product, which is designed to be injected into the urethral wall to reduce or eliminate the incidence of urinary incontinence. We are conducting pre-clinical research on the application of our MatrX Microspheres tissue-bulking product for stress urinary incontinence.

- **Vesicoureteral Reflux.** Vesicoureteral reflux is a condition in which urine may backflow from the bladder through the ureter and into the kidneys. This condition, which can result in urinary tract infections, pain, fever and discomfort, affects over one percent of children. We are conducting preclinical research on the application of MatrX Microspheres to bulk the area of tissue at the junction of the ureter and bladder to increase backflow resistance.

- Gastroesophageal Reflux Disease. Gastroesophageal reflux disease occurs when the stomach contents abnormally flow upward into the esophagus, which can lead to pain and esophageal ulcers. In many cases, gastroesophageal reflux disease is attributable to decreased tone of the lower esophageal muscle tissue or to a congenitally small band of muscle tissue. We are conducting research on how MatrX Microspheres tissue-bulking product, injected directly into the esophageal muscle tissue, improves its function.

GenS²™ Microspheres Injectable Tissue Scaffold

We are researching the use of GenS² Microspheres injectable tissue scaffold products for such applications as cartilage repair and other tissue or organ replacement. Several companies are developing and marketing bioartifical cells, tissues and supporting scaffoldings that hold the cells or tissues together. However, the existing tissue scaffoldings are either difficult to inject into the body, are digested by the body over time or do not adequately merge into the original tissue. In addition, most procedures still require surgery to implant the bioartifical tissues.

We believe that our microsphere technology can be formulated into injectable microsphere scaffolds, which we call GenS² Microspheres, which may overcome many of the limitations of tissue scaffolds currently commercially available. We are designing this product to adhere to cells and to be small enough to be injected, yet large enough to avoid digestion after injection.

Other Non-Strategic Products

In addition to our Embosphere Microspheres products, we sell barium delivery kits and other ancillary products in the European Union. Barium is purchased from Guerbet Medical, Inc. and resold for use in gastrointestinal medical testing. We sell other ancillary devices as medical products for hospital and physician use. While we generated a significant portion of our revenue in 2001 and 2000 from these non-strategic products, we do not expect these products to be a significant component of our future sales.

MARKETING AND SALES

We currently market our embolotherapy products through direct sales efforts in the United States and Canada and through a combination of direct sales, distributors, field representatives and direct marketing support in the European Union and other parts of the world. We are in the process of expanding our sales and marketing presence in the European Union, the United States and Japan. In January 2002, we entered into an exclusive pan-European distribution agreement with Terumo Europe N.V., a wholly owned subsidiary of Terumo Corporation. Terumo is a world leader in developing, manufacturing and marketing cardiovascular and interventional radiology products, including microcatheters, guidewires and introducer systems that directly complement our embolization products. Terumo Europe will use its large direct sales and marketing team to develop markets and sell our microspheres in the European markets.

We plan to attend major medical conventions throughout the world pertaining to our targeted markets and invest in market development, including physician training and patient outreach. We are working closely with major academic centers to serve as centers for excellence for physician training, product evaluation and ongoing research. Many members of our Medical Advisory Board are associated with these major academic centers.

RESEARCH AND DEVELOPMENT

Our research and development group consists of ten employees and three consultants. In addition, we have several development agreements with outside product development contractors and study agreements with several medical centers.

Our research and development group is focusing on developing our product technology in three areas:

- continuous improvement of our core technology;
- new embolotherapy materials and platforms;

- complementary embolotherapy products; and
- new initiatives aimed at leveraging our core technology in new market areas.

Our core technologies include microsphere technologies, organic and inorganic polymer and surface chemistries for microsphere design and development, non-viral DNA transfection technology, and expertise and know-how in microsphere manufacturing.

During the fiscal years ended December 31, 2001, 2000 and 1999, we spent approximately $4.76 million, $2.52 million and $968,000, respectively on our research and development efforts. We expect our research and development expenses to increase in the future as we seek to increase our research and development staff and related facilities, enhance our existing products and develop additional products.

COMPETITION

Passive Embolotherapy

The primary competitive embolotherapy product sold by competitors is polyvinyl alcohol, or PVA, a product introduced into the market more than 20 years ago. We encounter, and expect to continue to encounter, competition in the sale of our current and future passive embolotherapy products. Our principal competitors in the field of passive embolotherapy are Boston Scientific Corporation, Cook Incorporated and Cordis Corporation, a Johnson & Johnson company, as well as companies selling or developing non-embolotherapy solutions for the disease states targeted by us. These competitors have, and our future competitors are likely to have, greater financial, operational, sales and marketing resources and more experience in research and development than we have. We compete primarily on the basis of product performance, ease of use, degree of targeted embolization control, and quality of patient outcome. Our future success will depend in large part on our ability to gain market leadership at the early stage of the development and acceptance of new procedures, and our ability to continue to develop and bring to market differentiated products enhancing embolotherapy.

Active Embolotherapy

Although we are not aware of any company selling or marketing active embolotherapy products, we expect to encounter competition in the future sale of any active embolotherapy products. We expect that our future competitors in this area may have greater financial, operational, sales and marketing resources and more experience in research and development than we have. In addition, we expect to compete with companies that are developing and marketing other anticancer therapies and gene therapy drugs. These competitors include several large pharmaceutical companies along with numerous smaller biotechnologies. We believe that the principal competitive advantages in the active embolotherapy market will include the ability to deliver a highly concentrated dose of gene or drug to the tumor without negatively affecting other parts of the body, product designs facilitating a minimally invasive outpatient procedure, and a sales and marketing organization which is able to support specialized physician groups.

Tissue Bulking and Tissue Engineering

In the field of tissue bulking and tissue engineering, we believe that competition will come from companies that are currently developing and marketing tissue bulking, tissue repair and regeneration products. We believe our principal competitors in the field of tissue engineering are companies such as Boston Scientific Corporation, CR Bard, Inc., Johnson & Johnson and Medtronic, Inc. These competitors have, and our future competitors are likely to have, greater financial, operational, sales and marketing resources and more experience in research and development than we have. We believe that the principal competitive advantages in the tissue engineering market will be the ability to obtain durable effects while reducing the invasiveness of the procedure.

GOVERNMENT REGULATION

FDA Regulation. The FDA, and other federal, state, local, and foreign authorities, regulate our products and manufacturing activities. Pursuant to the Federal Food, Drug, and Cosmetic Act and the regulations promulgated thereunder, the FDA regulates the development, clinical testing, manufacture, packaging, labeling, storage, distribution and promotion of medical devices. Before a new device can be introduced into the market, the manufacturer must generally obtain marketing clearance through a 510(k) notification or approval through a premarket approval application. We generally will be required to obtain 510(k) clearance or premarket approval prior to commercial distribution of future products or additional applications of current products. Our proposed active embolotherapy products will likely be regulated as combination products, meaning they could be subject to regulation similar to drugs as well as devices, which may involve more extensive clinical testing and a more rigorous FDA review process than required for our microspheres and ancillary products, and other proposed products.

Classification of Medical Devices. In the United States, medical devices intended for human use are classified into three categories, Class I, II, or III, on the basis of the controls deemed reasonably necessary by the FDA to assure their safety and effectiveness. Class I devices are subject to general controls, for example, labeling, adherence to the FDA's Good Manufacturing Practice regulations and in some instances, premarket notification under Section 510(k). Class II devices are subject to general and special controls, for example, performance standards, postmarket surveillance, patient registries, and FDA guidelines. Class III is the most stringent regulatory category for medical devices. Many Class III devices are subject to premarket approval requirements. Class III devices include, for example, devices which are life-sustaining, or life-supporting, or new devices which have not been found substantially equivalent to legally marketed devices.

510(k) Clearance. The FDA will clear a device under section 510(k) if the submitted information establishes that the proposed device is substantially equivalent to a legally marketed Class I or II medical device, or to a Class III medical device for which the FDA has not yet called for a premarket approval application. Commercial distribution can begin only after the FDA issues an order finding that the device is substantially equivalent to a device that is legally marketed and not subject to a premarket approval requirement. The 510(k) notice may have to be supported by laboratory testing, animal testing and/or clinical testing. The FDA may determine that a proposed device is not substantially equivalent to a legally marketed device, in which case a premarket approval will be required to market the device, unless additional information can be submitted to support a substantial equivalence determination, or the FDA, pursuant to a timely request from a 510(k) submitter, makes a risk-based determination that a not-substantially-equivalent device can be classified into Class I or II. An FDA request for additional data could require that clinical studies of the device's safety and effectiveness be performed. In April 2000, we received 510(k) clearance to market Embosphere Microspheres for embolization of hypervascularized tumors and arteriovenous malformations. Our embolotherapy device is classified into Class III by the FDA, which means that even though we obtained 510(k) clearance to market the device, the FDA could issue a proposed rule and, subsequently, promulgate a regulation requiring premarket approval of the device to allow it to remain on the market or could require premarket approval for new treatment indications for the device. A requirement for premarket approval will likely require us to continue costly clinical trials and there is no guarantee that we can provide the FDA sufficient data for premarket approval in a timely fashion, if at all. Failure to obtain premarket approval would result in removal of our product from the United States market.

If human clinical trials of a device are required, and the device presents a "significant risk," the sponsor, usually the manufacturer or the distributor of a device, must obtain FDA approval of an investigational device exemption application prior to commencing human clinical trials. Sponsors of clinical trials are permitted to charge for devices distributed in the course of a study provided such charges do not exceed recovery of the costs of manufacture, research, development and handling, but devices may not be commercialized, e.g., promoted as safe or effective. The study must comply with the FDA's investigational device exemption regulations or other regulations. The sponsor must also obtain approval from one or more institutional review boards. Investigational device exemption trials are subject to extensive regulation, and may be placed on hold or terminated by the FDA if, among other reasons, there is reason to believe the risks do not outweigh the anticipated benefits. The clinical trial process may take years.

Premarket Approval. A premarket approval application must be filed and approved before a device can be marketed if a proposed device is not substantially equivalent to a legally marketed device or, as discussed above, if it is a pre-amendments Class III device, i.e., a device in commercial distribution prior to May 28, 1976, for which the FDA has called for premarket approvals. A premarket approval application must be supported by valid scientific evidence, which typically includes extensive data, including pre-clinical and clinical trial data, to demonstrate the safety and effectiveness of the device. Obtaining approval can take several years and approval may be conditioned on, among other things, substantial restrictions on indications for use and the conduct of postmarket surveillance studies.

The FDA has not formally decided how it will conduct the premarket review for the use of embolic particles for uterine fibroid embolization. The FDA may decide to require a premarket approval application or, alternatively, may allow commercial clearance via a 510(k) notice together with clinical support that substantiates product safety and efficacy. We have received an investigational device exemption pursuant to which we are conducting clinical studies to investigate the safety and efficacy of the Embosphere Microspheres for uterine artery embolization. We intend to file for marketing clearance under the 510(k) process unless the FDA requires a premarket approval application.

Drug Regulations: Drug and device approvals require extensive clinical testing involving multiple phases. The clinical data must demonstrate, from adequate and well-controlled trials, that the drug or device, as the case may be, is safe and effective in order to obtain approval. Clinical trials typically take years to complete. Before initiating such a clinical trial, we must obtain an investigational new drug exemption, or INDA, from FDA.

Changes in Approved Devices. Device manufacturers must obtain new FDA 510(k) clearance when there is a major change or modification in the intended use of a legally marketed device or a change or modification, including product enhancements, to a legally marketed device that could significantly affect its safety or effectiveness. Supplements for approved premarket approval devices are required for device changes, including some manufacturing changes that may affect safety or effectiveness. For devices marketed pursuant to 510(k) determinations of substantial equivalence, we must obtain FDA clearance of a new 510(k) notification prior to marketing the modified device; for devices marketed with premarket approval, we must obtain FDA approval of a supplement to the premarket approval prior to marketing the modified device.

Good Manufacturing Practices and Reporting. The Federal Food, Drug, and Cosmetic Act requires us to comply with Good Manufacturing Practices or Quality Systems regulations. We must comply with various quality control requirements pertaining to all aspects of our product design and manufacturing process including requirements for packaging, labeling and record keeping, including complaint files. The FDA enforces these requirements through periodic inspections of medical device manufacturing facilities. In addition, the Medical Device Reporting regulation obligates us to inform the FDA whenever information reasonably suggests that one of our devices may have caused or contributed to death or serious injury, or when one of our devices malfunctions, if the device would be likely to cause or contribute to a death or a serious injury in the event the malfunction recurred.

Labeling and Advertising. Labeling and promotional activities are also subject to scrutiny by the FDA. Among other things, labeling is violative of the law if it is false or misleading in any respect or it fails to contain adequate directions for use. Moreover, claims that are outside the labeling either approved or cleared by the FDA may violate the Federal Food, Drug, and Cosmetic Act.

Our product promotion is also subject to regulation by the Federal Trade Commission under the Federal Trade Commission Act, which prohibits unfair methods of competition and unfair or deceptive acts or practices in or affecting commerce, as well as unfair or deceptive practices such as the dissemination of any false advertisement pertaining to medical devices. Under the Federal Trade Commission's substantiation doctrine, an advertiser is required to have adequate data for all product claims at the time the claims are first used in advertising or other promotions.

Import Requirements. To import a device, the importer must file an entry notice and bond with the U.S. Customs Department pending an FDA decision on the product's admissibility. All devices are subject to FDA examination before release from Customs. Any article that appears to be in violation of the Federal Food, Drug, and Cosmetic Act may be refused admission and a notice of detention and hearing may be issued. A product also can be detained without physical examination if the product has a past history or other information indicates that it may be violative. A device must have received 510(k) clearance or be subject to an approved premarket approval application if required.

Export Requirements. Products for export from Europe and from the United States are subject to foreign countries' import requirements and the FDA's or European regulating bodies' exporting requirements. The introduction of our products in foreign markets may subject them to foreign regulatory clearances, which may impose additional product standards, packaging and labeling requirements and import restrictions on devices. Regulatory requirements to market devices vary from country to country. In addition, each country has its own tariff regulations, duties, and tax requirements.

In addition to the import requirements of foreign countries, we must also comply with the United States laws governing the export of products regulated by the FDA. Devices that have obtained 510(k) clearance or premarket approval and comply with the law in all other respects may be exported without further FDA authorization. However, foreign countries often require, among other things, an FDA certificate for products for export. To obtain this certificate, the device manufacturer must certify to the FDA that the product has been granted clearance or approval in the United States and that the manufacturing facilities appeared to be in compliance with Good Manufacturing Practices regulations at the time of the last FDA inspection.

Under the FDA Export Reform and Enhancement Act of 1996, an unapproved device requiring a premarket approval or a device subject to an investigational device exemption may be exported to any country if the product complies with the laws of that country and has valid marketing authorization in one of the following countries or authorities: Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, the European Union, or a country in the European Economic Community, or EEC, if the device is marketed in an EEC country or authorized for general marketing in the EEC. The FDA is authorized to add countries to this list in the future. Further, a device may be exported under this provision only if, among other things, it meets the specifications of the foreign purchaser, complies with the laws of the importing country, is labeled for export, is manufactured in substantial compliance with Good Manufacturing Practices regulations or recognized international standards, is not sold in the United States, and meets other conditions.

Fines and Penalties for Noncompliance. Failure to comply with applicable FDA regulatory requirements could result in, among other things, premarket clearance or approval withdrawal, injunctions, product withdrawals, voluntary or mandatory patient/physician notifications, recalls, warning letters, product seizures, civil penalties, fines and criminal prosecutions. In addition, the Federal Trade Commission has a variety of processes and remedies available to it for enforcement, both administratively and judicially, including compulsory process, cease and desist orders and injunctions. Federal Trade Commission enforcement can result in orders requiring, among other things, limits on advertising, corrective advertising, consumer redress, rescission of contracts and such other relief as may be deemed necessary. Violation of such orders could result in substantial financial or other penalties. Any such action by the FDA or the Federal Trade Commission could materially adversely affect our ability to successfully market our products.

Medical device laws are also in effect in many countries outside of the United States. These range from comprehensive device approval requirements for some or all of our medical device products to simpler requests for product data or certification. The number and scope of these requirements are increasing. Sales of medical devices in the European Union are subject to the European Medical Device Directive. This directive contains requirements for quality system and product performance guidelines to which all manufacturers must comply. These guidelines contain quality system guidelines and preproduction product design verification that closely resemble current FDA guidelines. In 1997, we obtained ISO 9002 international quality systems registration, a

certification showing that our procedures and manufacturing facilities comply with standards for quality assurance and manufacturing process control. Our compliance with this registration has been confirmed since 1997 in semi-annual surveillance audits. In January 2002, we obtained certification to EN46001/ISO9001, which along with the manufacturing and quality controls of ISO9002, also adds design control requirements. The EN46001/ISO 9001 certification and the European Medical Device Directive Certification signifies compliance with the requirements, enabling us to affix the CE Mark to our Embosphere Microsphere and our EmboGold Microsphere product. The CE Mark denotes conformity with European standards for safety and allows certified devices to be placed on the market in all European Union countries. Medical devices may not be sold in European Union countries unless they display the CE Mark.

Failure to comply with applicable federal, state and foreign medical device laws and regulations would likely have a material adverse effect on our business. In addition, federal, state and foreign regulations regarding the manufacture and sale of medical devices are subject to future changes. We cannot predict what impact, if any, such changes might have on our business, but such change could have a material impact.

We are subject to various federal, state, local and foreign laws and regulations relating to the protection of the environment, as well as health and safety. In the course of our business, we are involved in the handling, storage and disposal of certain chemicals. The laws and regulations applicable to our operations include provisions that regulate the discharge of materials into the environment. Usually these environmental laws and regulations impose "strict liability," rendering a person liable without regard to negligence or fault on the part of such person. Such environmental laws and regulations may expose us to liability for the conduct of, or conditions caused by, others, or for acts that were in compliance with all applicable laws at the time the acts were performed. We do not believe that we have been required to expend material amounts in connection with our efforts to comply with environmental requirements or that compliance with such requirements will have a material adverse effect upon our capital expenditures, results of operations or competitive position. Failure to comply with applicable environmental and related laws could have a material adverse effect on our business. In addition, because the requirements imposed by such laws and regulations are frequently changed, we are unable to predict the cost of compliance with such requirements in the future, or the effect of such laws on our capital expenditures, results of operations or competitive position.

PROPRIETARY TECHNOLOGY AND PATENT RIGHTS

We seek to establish and protect our proprietary technologies and products through a combination of patent, copyright, trademark and trade secrets laws, as well as confidentiality provisions in our contracts. We have implemented a patent strategy designed to maximize our intellectual property rights. We are pursuing patent coverage in the United States and foreign countries to protect the technology, inventions and improvements that we consider critical to the development of our products and business.

In January 1998, we entered into an agreement with L'Assistance Publique-Hopitaux De Paris, referred to as AP-HP, pursuant to which AP-HP has granted us the exclusive right to use two jointly-owned patents relating to micospheres. We are required to pay to AP-HP a royalty on the commercial sale of any products, which incorporate technology covered by the patents. We may only sublicense these exclusive rights under the agreement with the prior written consent of AP-HP, which consent cannot be unreasonably withheld. The rights granted under the contract are for an initial period, which ends on September 16, 2009, and are renewable by mutual agreement between the parties. The agreement can be terminated on three months notice by either party if the other party does not perform one or more of its obligations under the agreement and fails to cure its nonperformance during the notice period. These jointly-owned patents will expire in 2014.

In addition, as part of the sale of our former core business to Invitrogen, Inc., formerly know as Life Technologies, in May 1999, we entered into a cross-license agreement with Invitrogen. Under that agreement, Invitrogen has granted to us an exclusive, worldwide, perpetual, royalty-free license to its technology and patents relating to our core field of development, including any improvement to that technology made prior to May 2004.

Under the agreement, we also granted to Invitrogen an exclusive, worldwide, perpetual, royalty-free license to any improvements to the technology they have licensed to us, which are useful in Invitrogen's fields of development. Either party can terminate the agreement, and all licenses granted thereunder on sixty day's notice in the event of a breach of the agreement by the other party.

In 1999, we entered into an agreement with Dr. Shinichi Hori, pursuant to which we have an exclusive royalty-bearing license to Japanese patent rights for our Hepasphere SAP Microsphere product. These patent rights expire in 2012. There are no United States or other international filings corresponding to this patent application. We intend to file patent applications directed to improvement of this inventor's technology. However, present applications may not issue as patents, and these patents, if issued, may not provide us with sufficient protection against competitors. Further, we may be required to obtain additional licenses concerning the Japanese patent application and any licenses, if obtained, may not be on terms that are acceptable to us.

We were recently granted a United States patent directed to the treatment of urinary incontinence using microparticles. This patent expires in March 2019.

We have filed two patent applications relating to materials and methods for active embolotherapy, gene therapy and the treatment of gastroesophageal reflux disease, urinary incontinence and skin wrinkles. In addition, in July 1999, we entered into an agreement with the Louis Pasteur University in Strasbourg, France and Centre National de la Recherche Scientifique pursuant to which we received exclusive, royalty-bearing worldwide rights to two United States patents relating to active embolotherapy technology. We have filed a patent application relating to our material, formulation process and method of use for our new EmboGold Microspheres.

We have filed four United States patent applications and corresponding foreign applications relating to the use of embolotherapy for tissue bulking and the treatment of urinary incontinence, vesicoureteral reflux, dermal augmentation, skin wrinkles and gastroesophageal reflux disease. We have also filed patent applications relating to materials and methods for tissue regeneration.

Our success depends to a significant degree upon our ability to develop proprietary products and technologies and to obtain patent coverage for these products and technologies. We intend to continue to file patent applications covering any newly-developed products and technologies. However, as discussed above, there can be no guarantee that any of our pending or future filed applications will be issued as patents. There can be no guarantee that the United States Patent and Trademark Office or some third party will not initiate an interference proceeding involving any of our pending applications or issued patents. Finally, there can be no guarantee that our issued patents or future issued patents, if any, will provide adequate protection from competition, as further discussed below.

Patents provide some degree of protection for our proprietary technology. However, the pursuit and assertion of patent rights, particularly in areas like medical device development, involve complex legal and factual determinations and, therefore, are characterized by significant uncertainty. In addition, the laws governing patent issuance and the scope of patent coverage continue to evolve, particularly in life sciences. Moreover, the patent rights we possess or are pursuing generally cover our technologies to varying degrees. As a result, we cannot assure you that patents will issue from any of our patent applications or from applications licensed to us or that any of our issued patents will offer meaningful protection. In addition, our issued patents or patents licensed to us may be successfully challenged, invalidated, circumvented or rendered unenforceable so that our patent rights may not create an effective competitive barrier. Moreover, the laws of some foreign countries may not protect our proprietary rights to the same extent, as do the laws of the United States. There can be no assurance that any patents issued to us will provide a legal basis for establishing an exclusive market for our products or provide us with any competitive advantages or that the patents of others will not have an adverse effect on our ability to do business or to continue to use our technologies freely. In view of these factors, the value of our intellectual property position is uncertain.

We may be subject to third parties filing claims asserting that our technologies or products infringe on their intellectual property. We cannot predict whether third parties will assert such claims against us or our licensees or against the licensors of technology licensed to us, or whether those claims will harm our business. If we are forced to defend against such claims, regardless of their merit or whether they are resolved in favor of or against us, our licensees or our licensors, we may face costly litigation and diversion of management's attention and resources. As a result of such disputes, we may have to develop, at a substantial cost non-infringing technology, or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to us, or at all, which could seriously harm our business or financial condition.

We also rely in part on trade secret protection of our intellectual property. We attempt to protect our trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Our employees also sign agreements requiring that they assign to us their interests in inventions and original expressions and any corresponding patents and copyrights arising from their work for us. However, it is possible that these agreements may be breached, invalidated or rendered unenforceable and if so our trade secrets could be disclosed to others, including our competitors, and there may not be an adequate corrective remedy available. Despite the measures we have taken to protect our intellectual property, parties to our agreements may breach the confidentiality provisions in our contracts or infringe or misappropriate our patents, copyrights, trademarks, trade secrets and other proprietary rights. In addition, third parties may independently discover or invent competitive technologies or reverse engineer our trade secrets, or other technology. Therefore, the measures we are taking to protect our proprietary technology may not be adequate.

EMPLOYEES

As of February 28, 2002, we employed 87 persons. Of these employees, 10 are primarily engaged in research and development activities, 20 are engaged in manufacturing, 38 are engaged in sales and marketing, and the remainder are engaged in finance and administration. Of these 87 persons, 44 are located in the United States, 41 are located in France and 2 are located in Japan.

Our employees in the United States are not covered by a collective bargaining agreement. In Europe, our employees are covered by the provisions of an agreement setting forth national guidelines and standards for labor relations within our industry. We consider our relations with our employees to be good.

RISK FACTORS THAT MAY AFFECT FUTURE OPERATING RESULTS

This Annual Report on Form 10-K contains forward-looking statements. For this purpose, any statements contained herein that are not statements of historical fact may be considered to be forward-looking statements. Although not a complete list of words that might identify forward-looking statements, we use the words "believes," "anticipates," "plans," "expects," "intends," and similar expressions to identify forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated by forward-looking statements. Factors that could cause or contribute to such differences include those discussed below, as well as those discussed elsewhere in this Form 10-K. We expressly disclaim any obligation to update or alter our forward-looking statements, whether as a result of new information, future events or otherwise.

RISK RELATING TO OUR FUTURE PROFITABILITY

Because we have a history of losses and our future profitability is uncertain, our common stock is a highly speculative investment

We have incurred operating losses since our inception and, as of December 31, 2001, had an accumulated deficit of approximately $54.9 million. We expect to spend substantial funds to continue research and product testing, to establish sales, marketing, quality control, regulatory and administrative capabilities and for other general corporate purposes. We expect to continue incurring losses for the next fiscal year as we expand our commercialization efforts.

We may never become profitable. If we do become profitable, we may not remain profitable on a continuing basis. Our failure to become and remain profitable would depress the market price of our common stock and impair our ability to raise capital and expand, diversify or continue our operations.

RISKS RELATING TO OUR INDUSTRY, BUSINESS AND STRATEGY

If we do not achieve widespread market acceptance of our Embosphere Microspheres product, our business prospects will be seriously harmed

Our Embosphere Microspheres are based on new technologies and therapeutic approaches. In the United States, we only recently began selling our Embosphere Microspheres product for the embolization of hypervascularized tumors and arteriovenous malformations. We will require additional FDA approval before we can market Embosphere Microspheres in the United States for use in the embolization of uterine fibroids. Our success will depend upon the medical community, patients and third party payors accepting our Embosphere Microspheres product as medically useful, cost-effective and safe. In particular, our success will depend upon obstetrics and gynecology physicians referring patients to interventional radiologists to receive treatment using our products in lieu of, or in addition to, receiving other forms of treatment that the obstetrics and gynecology physicians can otherwise provide directly.

Negative publicity associated with any adverse medical effects attributed to embolization treatments generally or our product specifically, may create the market perception that our products are unsafe. For example, patients commonly experience a day or two of post-procedure abdominal pain or cramping. Other infrequently occurring complications may include allergic reactions, rashes, early onset of menopause, infertility and infection that may, in some limited cases, require a hysterectomy. In addition, Embosphere Microspheres are designed to remain in the body permanently. As a result, there is some limited risk that some or all of the Embosphere Microspheres used in a medical procedure may travel in the blood system beyond the intended site of action and occlude, or block, other blood vessels, resulting in significant adverse health effects on the patient or even death. Moreover, to use our Embosphere Microspheres correctly for a particular medical procedure, physicians must select and use the proper size and quantity of Embosphere Microspheres. A physician's selection and use of the wrong size or quantity of Embosphere Microspheres could have significant adverse health effects on the patient, including death. It will be necessary for us to spend significant amounts of money and allocate management resources to educate physicians about the selection and use of the proper size and quantity of Embosphere Microspheres in patient therapy. In addition, there is only limited data concerning the long-term health effects on persons resulting from embolotherapy using our Embosphere Microspheres.

If we are not able to successfully educate physicians to properly use our product or if the market determines or concludes that our product is not safe or effective for any reason, we may be exposed to product liability claims, product recalls and fines or other penalties or enforcement actions by regulatory agencies and associated adverse publicity. In addition, we have provided to our customers a satisfaction guarantee that requires us to accept the return of any inventory and credit the entire amount of the original order if a properly trained customer is not satisfied with the performance of our microspheres. If we experience adverse publicity or are subject to product liability claims, excessive guarantee claims, recalls, fines and the like, we will be unable to achieve widespread market acceptance of our Embosphere Microsphere products and achieve profitability.

We will be required to expend significant resources for research, development, testing and regulatory approval of our products under development and these products may not be developed successfully

We are developing and commercializing products for medical applications using embolotherapy techniques and also seeking to develop potential applications in several non-embolotherapy applications. Except for our Embosphere Microspheres product, most of our product candidates are still in the early stages of research and development. Our products may not provide greater benefits than current treatments or products, or than treatments or products under development. All of our products under development will require significant

additional research, development, pre-clinical and/or clinical testing, regulatory approval and a commitment of significant additional resources prior to their commercialization. Our potential products may not:

- be developed successfully;
- be proven safe and effective in clinical trials;
- offer therapeutic or other improvements over current treatments and products;
- meet applicable regulatory standards or receive regulatory approvals;
- be capable of production in commercial quantities at acceptable costs; or
- be successfully marketed.

If we do not develop, obtain marketing approvals and successfully introduce new products, we may not achieve revenue opportunities

We derived more than a majority of our revenue for the years ended December 31, 2001 and 2000 from the sale of Embosphere Microspheres. In addition, although we have not received FDA clearance or approval to market our Embosphere Microspheres for the specific use in the treatment of uterine fibroids, we believe that a majority of our revenue in the United States for the years ended December 31, 2001 and 2000 was derived from the sale of Embosphere Microspheres for use in uterine fibroid embolization. We derived approximately 19% of our revenue for the years ended December 31, 2001, and 49% of our revenue for the year ended December 31, 2000 from the sale of non-strategic products that we do not expect to constitute a significant portion of our revenue on an ongoing basis. Accordingly, we need to seek and obtain marketing approval for the use of Embosphere Microspheres for uterine artery embolization, develop and introduce new applications for our embolotherapy technology and pursue opportunities for microsphere technology in other medical applications. If we are not successful in these efforts, we may not achieve revenue opportunities.

If we experience delays, difficulties or unanticipated costs in establishing the sales, distribution and marketing capabilities necessary to successfully commercialize our products, we will have difficulty maintaining and increasing our sales

We are currently developing sales, distribution and marketing capabilities in the United States and have only limited sales, distribution and marketing capabilities in the European Union. It is expensive and time-consuming for us to develop a global marketing and sales force. Moreover, we may choose or find it necessary to enter into strategic collaborations to sell, market and distribute our products. The terms of any collaboration may not be favorable to us. We may not be able to provide adequate incentive to our sales force or to establish distribution and marketing collaborations with other companies to promote our products. We must also market our products in compliance with federal, state and local laws relating to the providing of incentives and inducements. Violation of these laws can result in substantial penalties. If we are unable to successfully motivate and expand our marketing and sales force and further develop our sales and marketing capabilities, or if our distributors fail to promote our products, we will have difficulty maintaining and increasing our sales.

If the strategic redirection of our business is not successful, we may be unable to achieve growth in our business

In early 1999, we decided to exit the chromatography business, which had constituted our core business, to focus on the commercialization of microspheres for use in embolotherapy and other medical applications.

We have restated our historical financial statements to reflect the discontinuation of our chromatography business. In addition, 73% of 1999 revenue, 49% of 2000 revenue and approximately 19% of revenue in 2001 included in our consolidated financial statements was derived from the sale of products we consider to be non-strategic and which we do not expect to constitute a significant portion of our revenue on an ongoing basis. Our strategic shift from the chromatography business to the commercialization of microspheres may not prove to be successful and, consequently, we may be unable to commercially develop our business and achieve profitability.

If we are unable to obtain adequate product liability insurance, then we may have to pay significant monetary damages in a successful product liability claim against us

The development and sale of medical devices entails an inherent risk of product liability. Product liability insurance is generally expensive for medical device companies such as ours. Although we maintain limited product liability insurance coverage for our products, it is possible that we will not be able to obtain further product liability insurance on acceptable terms, if at all. Insurance we subsequently obtain may not provide us with adequate coverage against all potential claims. If we are exposed to product liability claims for which we have insufficient insurance, we may be required to pay significant damages which would prevent or delay our ability to commercialize our products.

If we are not able to compete effectively, we may experience decreased demand for our products, which may result in price reductions

We have many competitors in the United States and abroad, including medical device and therapeutics companies, universities and other private and public research institutions. Our success depends upon our ability to develop and maintain a competitive position in the embolotherapy market. Our key competitors are Cordis Corporation, a Johnson & Johnson company, Boston Scientific Corporation and Cook Incorporated. These and many of our other competitors have greater capabilities, experience and financial resources than we do. As a result, they may develop products that compete with our Embosphere Microspheres product more rapidly or at less cost than we can. Currently, the primary products with which our Embosphere Microspheres compete for some of our applications are polyvinyl alcohol, polymerizing gels and coils. In addition, our competitors may develop technologies that render our products obsolete or otherwise noncompetitive.

We may not be able to improve our products or develop new products or technologies quickly enough to maintain a competitive position in our market and continue to commercially develop our business. Moreover, we may not be able to compete effectively, and competitive pressures may result in less demand for our products and impair our ability to become profitable.

If we fail to maintain, or in some instances obtain, an adequate level of reimbursement for our products by third-party payors, there may be no commercially viable markets for our products

The availability and levels of reimbursement by governmental and other third party payors affects the market for any medical device. We may not be able to sell our products profitably if reimbursement is unavailable or limited in scope or amount. Some insurance companies do not reimburse for embolization procedures. These third-party payors continually attempt to contain or reduce the costs of healthcare by challenging the prices that companies such as ours charge for medical products. In some foreign countries, particularly the countries of the European Union where our Embosphere Microspheres product is currently marketed and sold, the pricing of medical devices is subject to governmental control and the prices charged for our products have in some instances been reduced as a result of these controls. Additionally, in both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system. Further proposals are likely. These proposals, if adopted, could result in less revenue for us, and could affect our ability to raise capital and market our products.

If we do not retain our senior management, other key employees, scientific collaborators and advisors, we may not be able to successfully implement our business strategy

The loss of key members of our management team could harm us. We also depend on our scientific collaborators and advisors, all of whom have other commitments that may limit their availability to us. Our success is substantially dependent on the ability, experience and performance of these members of our senior management and other key employees, scientific collaborators and advisors. Because of their ability and experience, if we lose one or more of these individuals, we may not be able to successfully implement our business strategy.

If we do not attract and retain skilled personnel, we will not be able to expand our business

Our future success will depend in large part upon our ability to attract and retain highly skilled scientific, operational, managerial and marketing personnel, particularly as we expand our activities in clinical trials, the regulatory approval process and sales and manufacturing. We face significant competition for these types of persons from other companies, research and academic institutions, government entities and other organizations. Consequently, if we are unable to attract and retain skilled personnel, we will not be able to expand our business.

If we make any acquisitions, we will incur a variety of costs and may never successfully integrate the acquired business into ours

We may attempt to acquire businesses, technologies, services or products that we believe are a strategic complement to our business model. We may encounter operating difficulties and expenditures relating to integrating an acquired business, technology, service or product. These acquisitions may also absorb significant management attention that would otherwise be available for ongoing development of our business. Moreover, we may never realize the anticipated benefits of any acquisition. We may also make dilutive issuances of equity securities, incur debt or experience a decrease in the cash available for our operations, or incur contingent liabilities in connection with any future acquisitions.

Because Sepracor Inc. and our executive officers and directors own a significant amount of our common stock, they may be able to exert control over us

As of January 31, 2002, Sepracor Inc. beneficially owns approximately 25% of our outstanding common stock. In addition, as of January 31, 2002, our executive officers and directors beneficially owned, in the aggregate, approximately 9% of our outstanding common stock, excluding shares owned by Sepracor which some of our directors and executive officers may be deemed to beneficially own, but including shares issuable upon exercise of vested options and warrants. Two of our directors are executive officers of Sepracor. Sepracor and our executive officers and directors will have substantial control over all corporate actions requiring stockholder approval irrespective of how our other stockholders may vote, including:

- the election of directors;
- the amendment of charter documents;
- the approval of mergers and other significant corporate transactions, including a sale of substantially all of our assets; and
- the defeat of any non-negotiated takeover attempt that might otherwise benefit the public stockholders.

This ownership concentration could cause the market price of our common stock to decline. In addition, conflicts of interest between Sepracor and us may arise, including with respect to competitive business activities and control of our management and our affairs.

RISKS RELATING TO REGULATORY MATTERS

If we do not obtain the regulatory approvals required to market and sell our products, then our business will be unsuccessful and the market price of our stock will substantially decline

We are subject to regulation by government agencies in the United States and abroad with respect to the manufacture, packaging, labeling, advertising, promotion, distribution and sale of our products. For example, our products are subject to approval or clearance by the FDA prior to marketing in the United States for commercial use. Similar regulations exist in most major foreign markets, including the European Union and Asia. The process of obtaining necessary regulatory approvals and clearances will be time-consuming and expensive for us. If we do not receive required regulatory approval or clearance to market our products, we will not be able to develop and commercialize our products and become profitable, and the value of our common stock will substantially decline.

We are focusing our immediate product commercialization efforts on our Embosphere Microspheres. In April 2000, we obtained clearance from the FDA to market our Embosphere Microspheres in the United States for the embolization of hypervascularized tumors and arteriovenous malformations. However, before we can market Embosphere Microspheres in the United States for use in the embolization of uterine fibroids, we will require either FDA clearance of a premarket notification under Section 510(k) of the Federal Food, Drug, and Cosmetic Act, which we refer to as a 510(k) notification, or the more time consuming and expensive approval of a premarket approval application. We do not expect to receive the required clearance or approval for specific labeling for uterine fibroids until at least the last quarter of 2002, if at all. In order to obtain FDA clearance or approval to market our product for this indication, we are conducting clinical trials. We cannot assure you that the data resulting from this study will be considered by the FDA to be sufficient to permit clearance or approval. If we do not receive FDA clearance or approval to market our Embosphere Microspheres in the United States in the treatment of uterine fibroids, our business will be adversely affected.

If the FDA or other regulatory agencies place restrictions on, or impose additional approval requirements with respect to, products we are then marketing, we may incur substantial additional costs and experience delays or difficulties in continuing to market and sell these products

Even if the FDA grants us approval or clearance with respect to any of our products, it may place substantial restrictions on the indications for which we may market the product, which could result in lower revenues. The marketing claims we are permitted to make in labeling or advertising regarding our Embosphere Microspheres are limited to those specified in any FDA clearance or approval. For example, because our products are not specifically approved for labeling for use for uterine fibroids, we may not promote them for this use. However, we believe that a majority of our revenue in the United States for the years ended December 31, 2001 and 2000 was derived from the sale of Embosphere Microspheres for use in uterine fibroid embolization.

We may in the future make modifications to our Embosphere Microspheres or their labeling which we determine do not necessitate the filing of a new 510(k) notification. However, if the FDA does not agree with our determination, it will require us to make additional 510(k) filings for the modification, and we may be prohibited from marketing the modified product until we obtain FDA clearance. Similarly, if we obtain premarket approval, we may not be able to make product or labeling changes until we get FDA approval.

Further, the FDA has classified our embolotherapy device into Class III, which means that even though we have obtained clearance under Section 510(k) to market the device for certain indications, the FDA could in the future promulgate a regulation requiring premarket approval of the device under Section 515 of the Federal Food, Drug, and Cosmetic Act to allow it to remain on the market. We may experience difficulty in providing to the FDA sufficient data for premarket approval in a timely fashion, if at all. In addition, the FDA may require us to conduct a postmarket surveillance study which would require us to track specific elements of patient experience with our Embosphere Microspheres product after we have begun marketing it. If such a study revealed previously unknown adverse events or an unexpectedly high rate of adverse events, the FDA could place further restrictions on our marketing of the device, or rescind our clearance or approval.

Our products will be subject to continuing FDA requirements relating to quality control, quality assurance, maintenance of records, documentation, manufacturing, labeling and promotion of medical devices. We are also required to submit medical device reports to the FDA to report device-related deaths or serious injuries, as well as malfunctions, the recurrence of which would be likely to cause or contribute to a death or serious injury. These reports are publicly available.

If our clinical trials are not completed successfully, we will not be able to develop and commercialize our products

Although for planning purposes we forecast the timing of completion of clinical trials, the actual timing can vary dramatically due to factors such as delays, scheduling conflicts with participating clinicians and clinical institutions, the rate of patient accruals and the uncertainties inherent in the clinical trial process. In addition, we

may rely on academic institutions or clinical research organizations to supervise or monitor some or all aspects of clinical trials involving our products. Accordingly, we may have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own. In addition, we will need FDA approval to initiate some clinical trials, and the trials must be conducted in compliance with FDA regulations. Furthermore, clinical or regulatory issues may occur that will compel us to temporarily or permanently suspend our clinical trials. As a result of these factors, we or third parties may not successfully begin or complete our clinical trials and we may not make regulatory submissions or receive required regulatory approvals to commence or continue our clinical trials in the time periods we have forecasted, if at all. If we or third parties fail to commence or complete, or experience delays in, any of our planned clinical trials, then we are likely to incur additional costs and delays in our product development programs, and we may not be able to successfully develop and commercialize our products. If we incur costs and delays in our programs or if we do not successfully develop and commercialize our products, our stock price could decline.

If we fail to comply with regulatory laws and regulations, we will be subject to enforcement actions, which will affect our ability to market and sell our products and may harm our reputation

If we fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to less acceptance of our products by the market. These enforcement actions include:

- product seizures;
- voluntary or mandatory recalls;
- voluntary or mandatory patient or physician notification;
- withdrawal of product clearances or approvals;
- withdrawal of investigational device exemption approval;
- restrictions on, or prohibitions against, marketing our products;
- fines;
- restrictions on importation of our products;
- injunctions;
- civil and criminal penalties; and
- withdrawal of premarket approval or rescission of premarket notification clearance.

RISKS RELATING TO INTELLECTUAL PROPERTY

If we are unable to obtain patent protection for our products, their competitive value could decline

We may not obtain meaningful protection for our technology and products with the patents and patent applications that we own or license relating to our microsphere technology. In particular, the patent rights we possess or are pursuing generally cover our technologies to varying degrees, and these rights may not prevent others from designing products similar to or otherwise competitive with our Embosphere Microspheres and other products commercialized by us. For example, our U.S. patent directed to copolymers used to make our present Embosphere Microspheres expired in June 2001. Two other U.S. patents and their foreign equivalents are also directed to materials and methods for performing embolization. To the extent that our competitors are able to design products competitive with ours without infringing our intellectual property rights, we may experience less market penetration with our products and, consequently, we may have decreased revenues.

We do not know whether competitors have similar United States patent applications on file, since United States patent applications filed before November 28, 2000 or for which no foreign patents will be sought are secret until issued, and applications filed after November 28, 2000 are published approximately 18 months after their earliest priority date. Consequently, the United States Patent and Trademark Office could initiate interference proceedings involving our owned or licensed United States patent applications or issued patents. Further, there is a substantial backlog of patent applications at the United States Patent and Trademark Office, and the approval or rejection of patent applications may take several years.

We require our employees, consultants and advisors to execute confidentiality agreements. However, we cannot guarantee that these agreements will provide us with adequate protection against improper use or disclosure of confidential information. In addition, in some situations, these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors have prior employment or consulting relationships. Further, others may independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets. Our failure to protect our proprietary information and techniques may inhibit or limit our ability to exclude certain competitors from the market.

If we become involved in expensive patent litigation or other proceedings to enforce our patent rights, we could incur substantial costs and expenses or substantial liability for damages or be required to stop our product development and commercialization efforts

In order to protect or enforce our patent rights, we may have to initiate legal proceedings against third parties, such as infringement suits or interference proceedings. By initiating legal proceedings to enforce our intellectual property rights, we may also provoke these third parties to assert claims against us and, as a result, our patents could be narrowed, invalidated or rendered unenforceable by a court. Furthermore, we may be sued for infringing on the intellectual property rights of others. We may find it necessary, if threatened, to initiate a lawsuit seeking a declaration from a court regarding the proprietary rights of others. Intellectual property litigation is costly, and, even if we prevail, could divert management attention and resources away from our business.

The patent position of companies like ours generally is highly uncertain, involves complex legal and factual questions, and has recently been the subject of much litigation. We may not prevail in any patent-related proceeding. If we do not prevail in any litigation, we could be required to pay damages, stop the infringing activity, or obtain a license. Any required license might not be available to us on acceptable terms, or at all. In addition, some licenses may be nonexclusive, and therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license or are unable to design around a patent, we may be prevented from selling some of our products, which could decrease our revenue.

If any of our licenses to use third-party technologies in our products are terminated, we may be unable to develop, market or sell our products

We are dependent on various license agreements relating to each of our current and proposed products that give us rights under intellectual property rights of third parties. These licenses impose commercialization, sublicensing, royalty, insurance and other obligations on us. Our failure, or any third party's failure, to comply with the terms of any of these licenses could result in us losing our rights to the license, which could result in us being unable to develop, manufacture or sell products which contain the licensed technology.

RISKS RELATING TO OUR FINANCIAL RESULTS AND NEED FOR FINANCING

We will continue to need additional funds, and if additional capital is not available, we may have to limit, scale back or cease our operations

We may need to raise additional funds to develop and commercialize our products successfully. If we cannot raise more funds, we could be required to reduce our capital expenditures, scale back our product development, reduce our workforce and license to others products or technologies that we otherwise would seek

to commercialize ourselves. Although we are presently negotiating a credit line with a bank, we currently have no committed source of capital in the United States. We may seek additional funding through collaborative arrangements, borrowing money or the sale of additional equity securities. We may not receive additional funding on reasonable terms or at all. Any sales of additional shares of our capital stock are likely to dilute our existing stockholders.

Further, if we issue additional equity securities, the new equity securities may have rights, preferences or privileges senior to those of existing holders of our common stock. Alternatively, we may borrow money from commercial lenders, possibly at high interest rates, which will increase the risk of your investment in us.

If operating results fluctuate significantly from quarter to quarter, then our stock price may decline

Our operating results could fluctuate significantly from quarter to quarter. These fluctuations may be due to several factors including the timing and volume of customer orders for our Embosphere Microspheres, customer cancellations and general economic conditions. We also expect that our operating results will be affected by seasonality, since we expect our revenues to decline substantially in the third quarter of each year from the first two quarters of each year because we do a significant percentage of our business in the European Union, which typically experiences a slowdown of business during August. Due to these fluctuations, our operating results in some quarters may not meet the expectations of stock market analysts and investors. In that case, our stock price would probably decline.

In addition, a large portion of our expenses, including expenses for facilities, equipment and personnel, are relatively fixed. Accordingly, if our revenue declines or does not grow as much as we anticipate, we might not be able to improve our operating margins. In addition, we plan to significantly increase operating expenses in the next several years. Failure to achieve anticipated levels of revenue could therefore significantly harm our operating results for a particular fiscal period.

RISKS RELATING TO THE PRODUCTION AND SUPPLY OF OUR PRODUCTS

If we experience manufacturing delays or interruptions in production, then we may experience customer dissatisfaction and our reputation could suffer

If we fail to produce enough products at our own manufacturing facility or at a third-party manufacturing facility, we may be unable to deliver products to our customers on a timely basis, which could lead to customer dissatisfaction and could harm our reputation and ability to compete. We currently produce all of our Embosphere Microspheres products in one manufacturing facility in France and sub-contract a significant portion of the final packaging process to an independent contract manufacturer. We would likely experience significant delays or cessation in producing our products at either of these facilities if a labor strike, natural disaster, local or regional conflict or other supply disruption were to occur. If we are unable to manufacture our products at our facility in France, or package certain of our products with our contract manufacturer, we may be required to enter into arrangements with one or more alternative contract manufacturing companies. We have contingency plans to establish manufacturing in the United States in place but we could encounter delays or difficulties establishing relationships with alternate contract manufacturers or in establishing agreements on terms that are favorable to us. In addition, if we are required to depend on third-party manufacturers, our profit margins may be lower, which will make it more difficult for us to achieve profitability.

Also, manufacturers, including us, must adhere to the FDA's current Good Manufacturing Practices regulations, which are enforced by the FDA through its facilities inspection program. The manufacturers may not be able to comply or maintain compliance with Good Manufacturing Practices regulations. If our manufacturers fail to comply, their non-compliance could significantly delay our receipt of premarket approval or result in FDA enforcement action, including an embargo on imported devices. For a premarket approval device, if we change our manufacturing facility or switch to a third-party manufacturer we will be required to submit a premarket approval application supplement before the change is implemented.

Because we rely on a limited number of suppliers, we may experience difficulty in meeting our customers' demands for our products in a timely manner or within budget

We currently purchase key components of our Embosphere Microspheres from a variety of outside sources. Some of these components may only be available to us through a few sources. We generally do not have long-term agreements with any of our suppliers.

Our reliance on our suppliers exposes us to risks, including:

- the possibility that one or more of our suppliers could terminate their services at any time without penalty;
- the potential inability of our suppliers to obtain required components;
- the potential delays and expenses of seeking alternative sources of supply;
- reduced control over pricing, quality and timely delivery due to the difficulties in switching to alternative suppliers; and
- the possibility that one or more of our suppliers could fail to satisfy any of the FDA's required current Good Manufacturing Practices regulations.

Consequently, in the event that our suppliers delay or interrupt the supply of components for any reason, our ability to produce and supply our products could be impaired, which could lead to customer dissatisfaction.

RISKS RELATING TO OUR FOREIGN OPERATIONS

If we are unable to meet the operational, legal and financial challenges that we will encounter in our international operations, we may not be able to grow our business

Our operations are currently conducted primarily through our French subsidiary. Furthermore, we currently derive a significant portion of our revenue from the sale of our Embosphere Microspheres and other products in the European

Union. We are increasingly subject to a number of challenges, which specifically relate to our international business activities. Our international operations may not be successful if we are unable to meet and overcome these challenges, which would limit the growth of our business. These challenges include:

- failure of local laws to provide the same degree of protection against infringement of our intellectual property;
- protectionist laws and business practices that favor local competitors, which could slow our growth in international markets;
- potentially longer sales cycles to sell products, which could slow our revenue growth from international sales; and
- potentially longer accounts receivable payment cycles and difficulties in collecting accounts receivable.

Because we exchange foreign currency received from international sales into U.S. dollars and are required to make foreign currency payments, we may incur losses due to fluctuations in foreign currency translations

A significant portion of our business is conducted in the European Union Euro. We recognize foreign currency gains or losses arising from our operations in the period incurred. As a result, currency fluctuations between the U.S. dollar and the currencies in which we do business will cause foreign currency translation gains and losses, which may cause fluctuations in our future operating results. We do not currently engage in foreign exchange hedging transactions to manage our foreign currency exposure.

RISK RELATING TO OUR STOCK PRICE

Because the market price of our stock is highly volatile, investments in our stock could rapidly lose their value and we may incur significant costs from class-action litigation

The market price of our stock is highly volatile. As a result, investments in our stock could rapidly lose their value. In addition, the stock market often experiences extreme price and volume fluctuations, which affect the market price of many medical device companies and which are often unrelated to the operating performance of these companies.

Recently, when the market price of a stock has been as volatile as our stock price has been, holders of that stock have occasionally instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs in defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Item 2. PROPERTIES

We currently lease office and manufacturing facilities in Rockland, Massachusetts, and Roissy, France. Our Rockland, Massachusetts, office includes approximately 13,000 square feet of corporate offices and laboratory space pursuant to a five-year lease expiring in March of 2005. Our Roissy, France facility includes approximately 18,150 square feet of office, laboratory and manufacturing space and is leased through May 2010.

At our facility in France, we produce our Embosphere Microspheres and some ancillary disposable devices. Embosphere Microsphere production includes the synthesis of raw materials and third party manufactured intermediary compounds. For certain products currently sold in North America, final product packaging is performed by a contracted third-party within the United States under Good Manufacturing Practices manufacturing standards.

We believe that our currently-leased facilities in Rockland, Massachusetts and Roissy, France are suitable to meet our current requirements and that suitable additional or substitute space will be available to us on commercially reasonable terms, if needed in the future.

Item 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings.

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

No matters were submitted to a vote of security holders of the Company, through solicitations of proxies or otherwise, during the quarter ended December 31, 2001.

EXECUTIVE OFFICERS

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

Name	Age	Position
John M. Carnuccio	48	Chief Executive Officer, President and Director
Alain Brunier	57	President, Europe
Jonathan R. McGrath	47	Vice President, Worldwide Research and Development
Robert M. Palladino	47	Vice President and Chief Financial Officer
Robert T. Phelps	45	Vice President, U.S. Sales and Business Development
Michael Miley	39	Vice President, U.S. Marketing

John M. Carnuccio, age 48, has served as a director of BioSphere since June 1999. From January 1999 until May 1999, Mr. Carnuccio served as Executive Vice President of BioSphere and President of the Medical Products Business of BioSphere. In May 1999, he was appointed President and Chief Executive Officer of BioSphere. From 1979 to January 1999, Mr. Carnuccio served in a number of capacities at Boston Scientific Corporation, a worldwide manufacturer of medical devices for interventional medicine, most recently as Vice President, Market Development, Interventional Gynecology, from April 1998 to January 1999 and as Vice President and General Manager, Microvasive Urology Division from 1992 to April 1998.

Alain Brunier, age 57, has served as President, Europe since June 2000. From 1996 to May 2000, Mr. Brunier served as Managing Director, France & North Africa of St. Jude Medical, a manufacturer of pacemakers and other medical devices used by cardiologists. From 1990 to 1996, Mr. Brunier served as Vice President and Chief Executive, Europe, Middle East & Africa of Telectronics, a manufacturer of pacemakers and implantable defibrillators. Prior to 1990, Mr. Brunier has also held senior management positions at SMAD – HEMO France and Baxter-Travenol.

Jonathan R. McGrath, age 47, has served as Vice President, Worldwide Research and Development since August 1999. From 1995 to 1998, Mr. McGrath served as Vice President of Research and Development at Urologix, a urological device company. From 1990 to 1995, he served as Vice President of Research and Development at Schneider/Pfizer, a cardiovascular device company. From 1987 to 1990, Mr. McGrath served as the Vice President of Product Development & Operations at Harbor Medical, a surgical device company. From 1980 to 1987, Mr. McGrath held various positions at Boston Scientific Corporation, most recently as the Director of Metals Product Development.

Robert M. Palladino, age 47, has served as Chief Financial Officer and Vice President since December 1999. From March 1999 to December 1999, Mr. Palladino served as Vice President and Chief Financial Officer of Coretek, Inc., a fiber optics manufacturer. From 1995 to 1999, he served as Vice President of Finance at C.P. Clare Corporation, a multinational electronics firm. He also served as Assistant Treasurer at the Kendall Company, a health care manufacturer from 1991 to 1995.

Robert T. Phelps, age 45, has served as the Vice President, U.S. Sales and Business Development since August 1999. From 1998 to 1999 Mr. Phelps was self-employed as a strategic sales consultant. From 1993 to 1998, Mr. Phelps served as Vice President of Sales, Orthopedic Division at Johnson & Johnson, a pharmaceutical company. From 1990 to 1993, Mr. Phelps served as the Group Controller, Orthopedics Division at Johnson & Johnson.

Michael Miley, age 39, has served as Vice President, U.S. Marketing, since August 2001. From January 2001 to July 2001, Mr. Miley served as Senior Director of Worldwide Market Development for BioSphere. From August 2000 to December 2000, Mr. Miley was an independent consultant to BioSphere. From 1988 to 2000, Mr. Miley held various sales and marketing positions with Boston Scientific Corporation, most recently as Director of Marketing, International – Aneurysmal Therapies.

PART II

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

Our Common Stock has traded on the Nasdaq National Market from March 1994 through January 13, 1999 and from March 29, 2000 to the present. Our Common Stock traded on the National Association of Securities Dealers, Inc. OTC Bulletin Board from January 14, 1999 to March 28, 2000. As of March 15, 2002, there were approximately 128 stockholders of record of our Common Stock.

The following table shows the range of high and low sales prices per share of our Common Stock as reported on the Nasdaq National Market or the OTC Bulleting Board, as the case may be, for the last two fiscal years.

	2001	
	High	Low
First Quarter	$19.81	$ 9.50
Second Quarter	$19.00	$11.56
Third Quarter	$13.79	$ 6.96
Fourth Quarter	$11.56	$ 7.00

	2000	
	High	Low
First Quarter	$50.50	$ 6.00
Second Quarter	$31.38	$12.25
Third Quarter	$18.63	$10.50
Fourth Quarter	$14.56	$ 9.00

We have not paid any dividends on our Common Stock since our inception and do not intend to pay any dividends in the foreseeable future.

Item 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes to those statements and other financial information included elsewhere in this Annual Report on Form 10-K.

Year Ended December 31,	2001	2000	1999	1998	1997
(In thousands, except per share amounts)					
Statement of Operations Data:					
Revenue:					
Revenue from product sales	$ 8,752	$ 3,961	$ 2,263	$ 155	$ 117
License fees and collaboration revenue	250	—	3	47	35
Total Revenue	9,002	3,961	2,266	202	152
Costs and expenses:					
Costs of products sold	2,356	1,461	1,404	95	72
Research and development	4,755	2,517	968	34	34
Selling, general and administrative	12,839	7,847	4,003	1,364	1,195
Stock-based compensation to non-employees	—	1,261	—	—	—
Total costs and expenses	19,950	13,086	6,375	1,493	1,301
Loss from operations	(10,948)	(9,125)	(4,109)	(1,291)	(1,149)
Other income (expense):					
Interest income	794	715	234	30	32
Interest expense	(31)	(54)	(134)	(222)	(72)
Other	(160)	17	15	—	—
Net loss from continuing operations	$(10,345)	$ (8,447)	$(3,994)	$ (1,483)	$ (1,189)
Net loss from discontinued operations	—	—	(539)	(330)	(2,615)
Net loss	$(10,345)	$ (8,447)	$(4,533)	$ (1,813)	$ (3,804)
Basic and diluted net loss per common share from continuing operations	$ (0.89)	$ (0.87)	$ (0.47)	$ (0.17)	$ (0.14)
Basic and diluted net loss per common share from discontinued operations	—	—	(0.06)	(0.04)	(0.31)
Basic and diluted net loss per common share	$ (0.89)	$ (0.87)	$ (0.53)	$ (0.21)	$ (0.45)
Basic and diluted weighted average number of common shares outstanding	11,642	9,700	8,456	8,437	8,423

Balance Sheet Data as of December 31,	2001	2000	1999	1998	1997
(In thousands)					
Cash, cash equivalents and marketable securities	$ 23,119	$15,276	$ 5,368	$ 2,235	$ 2,370
Working capital	22,789	14,136	4,490	2,552	3,835
Total assets	29,984	19,306	7,496	12,664	12,787
Debt and minority interest acquisition obligation	303	575	945	82	164
Stockholders' equity	25,873	15,686	4,588	9,136	10,716

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

The following discussion of our financial condition and results of operations should be read in conjunction with the Consolidated Financial Statements and the related Notes included elsewhere in this report. Except for historical information contained herein, matters discussed in this report constitute forward-looking statements. We use the words "expects," "estimates," "intends," "plans," "should" and similar expressions to identify such forward-looking statements. Actual results could differ materially from those set forth in the forward-looking statements. In light of the substantial risks and uncertainties inherent in all future projections, our inclusion of forward-looking statements in this report should not be regarded as representations by us that our objectives or plans will be achieved. Many factors could cause our actual results, performance or achievements to differ materially from those in the forward-looking statements. Reference is made in particular to the risk factors set forth in the subsection Item 1. Business—"Risk Factors That May Affect Future Operating Results" *to this report and the discussions set forth below in this report under "Management's Discussion and Analysis of Financial Condition and Results of Operations."*

Overview

We are pioneering the use of our proprietary bio-engineered acrylic beads, known as microspheres, for medical applications using embolotherapy techniques and also to develop potential applications in several non-embolotherapy applications. Embolotherapy is a minimally invasive procedure in which embolic materials, such as our microspheres, are delivered through a catheter into the blood vessels to inhibit blood flow to tumors or vascular defects or to control blood loss presurgically. Our initial product, Embosphere Microspheres, is targeted for the treatment of hypervascularized tumors and arteriovenous malformations. Hypervascularized tumors are tumors that have a large number of blood vessels feeding them and include certain tumors affecting the brain and spinal cord, tumors in the uterus, known as uterine fibroids, and tumors associated with primary liver cancer. By selectively blocking the tumor's blood supply, embolotherapy is designed to cause the tumor to shrink and necrose. Based on preliminary research, we believe that our microsphere technology platform can also be adapted to deliver drugs, living tissue or genetic material to targeted sites.

BioSphere Medical, Inc. was originally incorporated in 1993 under the name BioSepra, Inc., as a chromatography media company. During 1999, we strategically refocused our business on the development and commercialization of our proprietary microspheres for medical applications. In February 1999, we acquired a 51% ownership interest in Biosphere Medical S.A., a French société anonyme, which we refer to as BMSA. Between April 2000 and November 2001, we acquired the remaining ownership interest in BMSA. BMSA retains the license to the embolotherapy device that is the main focus of our business. In May 1999, we sold substantially all of our assets relating to our former core business, chromatography, and changed our name to BioSphere Medical, Inc. As of December 31, 2001, Sepracor Inc., a specialty pharmaceutical company, beneficially owned approximately 25% of our outstanding common stock.

In April 2000, we received clearance from the United States FDA for embolization of hypervascularized tumors and arteriovenous malformations, excluding specific marketing approval for the uterine fibroids. In December 2000, we commenced our pivotal Phase II clinical testing, under an investigational device exemption, of the safety and effectiveness of treating uterine fibroids by uterine artery embolization with our Embosphere Microspheres. An investigational device exemption is a regulatory exemption granted by the FDA to medical device manufacturers for the purpose of conducting clinical studies. We intend, pending FDA clearance or approval for this indication, to promote our microspheres for the treatment of uterine fibroids. We do not anticipate receiving this clearance or approval before the last fiscal quarter of 2002, if at all.

We received CE mark approval of our Embosphere Microspheres product in the European Union in 1997. CE mark approval is a certification granted by European regulatory bodies, or by some manufacturers with satisfactory quality systems, that substantiates the compliance of products with specific standards of quality and/or safety. This approval is generally required prior to the commercialization of a medical device in the European Union. In January 2000, we received marketing approval of our Embosphere Microspheres product in Australia and Canada.

Our revenue is primarily generated from product sales of Embosphere Microspheres in the United States, European Union, Australia and Canada. Product revenues also include the sale of barium and other ancillary products manufactured by us or by third parties. Although we have not received FDA clearance or approval to market our Embosphere Microspheres for the specific use in the treatment of uterine fibroids, we believe that a majority of our revenue in the United States for the years ended December 31, 2001 and 2000 was derived from the sale of Embosphere Microspheres for use in uterine fibroid embolization.

During 2000, we established two wholly owned subsidiaries to pursue the development of other microsphere technologies. In April 2000, we established Biosphere Medical Japan, Inc., a Delaware corporation, to develop and commercialize Embosphere Microspheres as well as Hepasphere SAP Microspheres in Asia. In December 2000, we established BSMD Ventures, Inc., also a Delaware corporation, to explore and develop non-embolotherapy applications with a specific focus on tissue engineering uses.

We have experienced operating losses in each fiscal period since our inception. As of December 31, 2001, we had approximately $23.1 million in cash and short-term marketable securities and an accumulated deficit of approximately $54.9 million. In connection with the execution of our business plan, we expect to experience continued losses for the next fiscal year. The sale of our former chromatography business in 1999 has been presented in the financial statements in accordance with discontinued operations accounting principles. Accordingly, the results of all discontinued operations have been excluded from the continuing operations and presented separately in the accompanying selected financial data.

Critical Accounting Policies

The discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, revenues and expenses, and related disclosure at the date of our financial statements. Our significant accounting policies are summarized in Note B to our consolidated financial statements. The significant accounting policies which we believe are the most critical in gaining full understanding and evaluating our reported financial results include the following:

Revenue Recognition

Revenues from product sales are recognized when requested goods are shipped to customers and collection is considered probable. Management establishes reserves for potential sales returns and evaluates, on a monthly basis, the adequacy of those reserves based upon realized experience. Under our current policy, only those products on a customers' initial order qualify for credit returns. To date, returns have been minimal and immaterial. While such returns have historically been within our expectations and the provisions established, we cannot guarantee that we will continue to experience the same return rates that we have in the past. Any significant change in product satisfaction and any resulting credit returns could have a material adverse impact on our operating results for the period or periods in which such returns materialize.

Accounts Receivable

We continuously monitor collections and payments from our customers and maintain a provision for estimated credit losses based upon our historical payment experience and any specific customer collection issues that we have identified. While such credit losses have historically been within our expectations and the provisions established, we cannot guarantee that we will continue to experience the same credit loss rates that we have in the past. Substantially all of our receivables are due from hospitals, distributors, health care clinics, and managed care systems located throughout the United States, Australia, Canada, and Europe. A significant portion of products sold, both foreign and domestic, are ultimately funded through government reimbursement programs. As a consequence, changes in these programs can have an adverse impact on liquidity and profitability of our customer base.

Inventories

We value our inventory at the lower of the actual cost to purchase or manufacture the inventory. We regularly review inventory quantities in process and on hand and record a provision for production loss and obsolete inventory based primarily on actual loss experience and on our estimated forecast of product demand. Therefore, significant increases in the demand for our products could result in a short-term increase in production loss while a significant decrease in demand could result in an increase in the amount of excess inventory quantities on hand. In the future, if our inventory is determined to be overvalued, we would be required to recognize such costs in our costs of goods sold at the time of such determination. Likewise, if our inventory is determined to be undervalued, we would have over-reported our costs of goods sold in previous periods and would be required to recognize a reduced per unit cost at the time of sale. Therefore, although we make every effort to ensure the accuracy of our production process and forecasts of future product demand, any significant unanticipated changes in production yield or product demand could have a significant impact on the value of our inventory and our reported operating results.

Deferred Taxes

We use the asset and liability accounting method whereby deferred tax assets and liabilities are recognized based on temporary differences between the financial statements and tax bases of assets and liabilities using current statutory tax rates. A valuation allowance against net deferred tax assets is recorded if, based on the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Management evaluates, on a quarterly basis, the ability to recover the deferred tax assets and the level of the valuation allowance. Due to the size of our net operating loss carryforward in relation to our history of unprofitable operations we have not recognized any of our net deferred tax assets. We currently provide for income taxes only to the extent that we expect to pay cash taxes (primarily foreign subsidiary and certain state minimum net worth tax) for current income. However, future improvements in operational performance could result in the increased certainty of our ability to apply our deferred tax assets against taxable income which, could in turn, result in a significant impact on the value of our deferred tax assets and our reported operating results.

Results of Operations

Years Ended December 31, 2001, 2000 and 1999

Total revenue increased to $9.0 million for the year ended December 31, 2001 from $3.96 million for the same period in 2000 and $2.27 million in 1999. The $5.04 million increase from 2000 to 2001, as well as the $1.69 million increase from 1999 to 2000 is primarily due to an increase in sales of Embosphere Microsphere in the United Sates following receipt of FDA 510(k) clearance and commercial introduction in April 2000. North American revenues increased 394% from $1.27 million in 2000 to $6.27 million in 2001. No product sales were recorded in North America during 1999. Included in our 2001 consolidated and North American revenue was $250,000 in collaboration revenue recognized through a supply agreement with a third party. We expect that sales of our Embosphere Microspheres will continue to account for a majority of our revenue in 2002.

Costs of products sold for the year ended December 31, 2001 was $2.36 million, compared to $1.46 million in 2000 and $1.40 million in 1999, representing 27%, 37%, and 62% of product revenue, respectively. The $895,000 increase in the cost of product revenues in the year ended December 31, 2001 was due to increased sales volume offset by the effects of a shift in product sales to the Embosphere Microsphere products which have a higher gross profit margin than our other products.

Gross margin for the year ended December 31, 2001 was $6.65 million or 73% of product revenues compared with $2.5 million or 63% of product revenues for the same period in 2000 and $862,000 or 38% of product revenues in 1999. The increase in gross margin for each of the years ended December 31, 2001 and 2000 was attributable to the effects of a shift in the majority of sales to the higher margin Embosphere

Microsphere products, predominantly in North America. Also contributing to the gross margin improvement during 2001 and 2000 was the effect of improved manufacturing efficiencies and process improvements realized at our French production facility.

Research and development expenses increased to $4.76 million in 2001 from $2.52 million in 2000 and $968,000 in 1999. The $2.24 million increase from 2000 to 2001 as well as the $1.55 million increase in research and development expenses from 1999 to 2000 was due primarily to clinical trial and regulatory submission costs incurred relative to seeking regulatory approval for Embosphere Microsphere and EmboGold Microspheres in the United States. The 89% increase from 2000 to 2001 was also due to the final process development and validation costs incurred with respect to the release of our EmboGold Microspheres product line combined with additional salary and staffing expense in the United States. We anticipate future research and development expenses will increase as a result of the advancement of Embosphere Microsphere products through our pivotal Phase II clinical trial for uterine artery embolization of uterine fibroids, which was initiated in October 2000. The Phase II trial was approved by the FDA under an investigational device exemption. Additional expenses are also expected to result from the continued development and enhancement of our current products and product candidates.

Selling, general and administrative expenses, net of non-cash, non-employee stock option acceleration charges, increased to $12.84 million for the year ended December 31, 2001 from $7.85 million in 2000 and $4.0 million in 1999. The $4.99 million and $3.84 million increases in selling, general and administrative expenses from 2000 to 2001 and from 1999 to 2000, respectively, were primarily due to the implementation of our product commercialization plan, including salary and other related costs associated with increased personnel, sales and marketing, investor relations and all other expenses associated with developing and introducing a new product platform in both the North American and European territories. Future selling, general and administrative expenses are expected to increase consistent with the growth in our revenue and the embolization industry in general.

In connection with stock options previously issued to non-employee advisors, we recognized, in accordance with Emerging Issues Task Force Abstract 96-18 "*Accounting for equity instruments that are issued to other than employees for acquiring, or in conjunction with selling, goods or services*" (EITF 96-18), $1.26 million in non-employee compensation expense during the year ended December 31, 2000. The non-cash stock-based compensation charge has been presented as a separate line item within the Statement of Operations for the year ended December 31, 2000. The $1.26 million aggregate fair value of the non-employee stock options was derived from the Black-Scholes option-pricing model.

Interest income was $794,000 in the year ended December 31, 2001 compared to $715,000 in 2000 and $234,000 in 1999. The growth in interest income in each of the sequential years was due to the continued increase in the average-daily invested cash balances offset, to a limited extent, by reduced rates of return, particularly during fiscal 2001. Increased invested cash primarily resulted from the May 1999 sale of our discontinued chromatography operations resulting in net proceeds of approximately $9.6 million along with the net proceeds of $5.9 million, $11.8 million and $20.4 million from our February 2000, July 2000 and July 2001 equity placements, respectively.

Interest expense decreased from $134,000 in 1999 to $54,000 in 2000 and to $31,000 in 2001. This sequential decrease for each of 2001 and 2000 was primarily due to the retirement of our debt in the second quarter of 1999. Interest expense during 2001 primarily resulted from the cost of financing operational cash flow as well as certain capital leases. Interest expense in 2000 resulted primarily from non-cash interest charges generated from the potential obligation to purchase the remaining outstanding minority interest in BMSA. See Note C to the consolidated financial statements.

Other income and (expense) increased from $15,000 in 1999 to $17,000 in 2000, then decreased to ($160,000) in 2001. Other income and expense is primarily comprised of the foreign currency exchange gains and losses and to a limited extent, gains on the sale of idle assets. The $177,000 change from 2000 to 2001 was primarily due to foreign currency losses associated with our inter-company trade.

We have not recorded any tax benefit resulting from our operating losses as management believes the ability to realize and benefit against future taxable income is uncertain.

Net loss from continuing operations increased to $10.35 million for the year ended December 31, 2001 compared to $8.45 million in 2000 and $3.99 million in 1999. The increases are a direct result of the implementation of our strategic plan to develop, introduce and commercialize our EmboSphere Microspheres, EmboGold Microspheres, and other product lines both in the North American and European markets.

Liquidity and Capital Resources

We have historically funded our operations from product sales, net proceeds provided by public and private equity offerings, funds provided by the sale of our former chromatography business, funds provided by Sepracor, bank financing, equipment financing leases and to a lesser extent, the exercise of stock options. As of December 31, 2001, we had $23.12 million of cash, cash equivalents and marketable securities, an increase of $7.84 million from $15.28 million as of December 31, 2000. This increase primarily resulted from the net proceeds of $20.4 million from our public offering of common stock in July 2001 offset, to a limited extent, by cash used to fund operations. As of December 31, 2001, we had $22.79 million in working capital. We expect to finance our 2002 operations through product sales and existing cash balances.

For the year ended December 31, 2001, we used $10.77 million in operating cash primarily to fund our sales, marketing, research and product development activities and to finance working capital requirements. Cash used in operations is expected to decrease over the next twelve month period as anticipated increases in product revenues are expected to offset the Company's operational and product development expenditures.

Net cash used in investing activities was $14.75 million for the year ended December 31, 2001 and primarily represents our investment of cash in excess of current operational needs in marketable securities. We also used $953,000 in connection with the purchase of the remaining outstanding equity interest in BMSA. From this step-acquisition, our total ownership interest in BMSA increased from 85% to 100%. The remaining cash used in investing activities of approximately $1.25 million was used to purchase property and equipment relating to establishing full manufacturing capabilities at BMSA and to obtain office equipment and furnishings in our corporate headquarters in Rockland, Massachusetts. We anticipate future capital expenditures will increase over the next twelve-month period consistent with our plan to expand our manufacturing, sales and marketing presence in the United States, Europe, the Far East, Australia and Canada. If available on favorable terms, we expect to finance certain future fixed asset acquisitions through leasing arrangements.

Net cash provided by financing activities was $20.78 million for the year ended December 31, 2001. On July 3, 2001, we completed an underwritten public offering of 4.0 million shares of our common stock at $11.00 per share. Of the 4.0 million shares of common stock offered, we sold 2.0 million shares and Sepracor sold 2.0 million shares. Our net proceeds were approximately $20.4 million. Proceeds from the public offering will be used for working capital and general corporate purposes, including product commercialization and research and development. On August 6, 2001, Sepracor sold an additional 600,000 shares of our common stock pursuant to the exercise of the underwriter's over-allotment option. As a result of this offering, including the over-allotment, Sepracor's beneficial ownership interest in our outstanding common stock decreased from approximately 55% to approximately 25%. In both February 2000 and in July 2000, we completed private-equity placements resulting in the issuance of an aggregate of 1,868,787 shares of common stock for net proceeds of approximately $17.72 million. The February 2000 private-equity issuance included warrants to purchase a total of 163,468 shares of common stock with an exercise price of $20 per share. Cash provided by financing activities also includes $149,000 and $558,000 received in connection with the sale of common stock through the exercise of options granted under our incentive stock option plans during the years ended December 31, 2001 and 2000, respectively.

We believe that our existing cash and other working capital, including the approximate $23.12 million in cash, cash equivalents and marketable securities that we have as of December 31, 2001, will be sufficient to fund our operating and capital requirements, as currently planned, at least through the next twelve-month period.

However, our cash requirements may vary materially from those now planned due to changes in anticipated research and development efforts, the scope and results of pre-clinical and clinical testing, changes in the focus and direction of our research and development programs, competitive and technological advances, the timing and results of FDA regulatory review, the market's acceptance of any approved products, and other factors.

We expect to incur substantial additional costs, including costs related to ongoing research and development activities, pre-clinical studies, clinical trials, the expansion of our manufacturing, laboratory and administrative functions as well as costs relating to further commercialization activities. We may also need additional funds for possible strategic acquisitions of synergistic businesses, products and/or technologies. These additional funds may be raised from time to time through additional public or private sales of equity, through borrowings, or through other financings. There are no assurances that we will be able to obtain any additional funding that may be required on acceptable terms, if at all.

Borrowing Arrangement

In March 2000, BMSA entered into a €152,450 ($135,000 equivalent as of December 31, 2001) term loan with a French national bank that is payable over five years and accrues interest at 5.4% per annum. The total loan balance outstanding as of December 31, 2001 was approximately €104,000 or $92,000.

As a co-borrower under Sepracor's commercial bank facility, we had availability to borrow up to $2.0 million through a line of credit agreement. As a result of our July 2001 underwritten public offering, Sepracor's ownership of our outstanding common stock was reduced to less than 50%, thereby automatically terminating the co-borrowing arrangement. Because we are no longer a party to the loan agreement, which had no outstanding balance as of December 31, 2001, the bank released Sepracor's guaranty of our obligations to the bank and Sepracor terminated its related security interest in our assets.

Commitments

As of December 31, 2001, we have entered into two operating leases pursuant to the lease of our facilities in Rockland, Massachusetts and Roissy, France. The Rockland, Massachusetts lease expires in March of 2005 and the Roissy, France operating lease expires in May 2010. During 2001, we entered into several non-cancelable capital lease agreements with various equipment-financing companies, in connection with the acquisition of certain manufacturing and computer equipment. The leases have initial terms of 30 to 60 months with interest rates of 5.4% to 13.4%. All corresponding leased equipment serves as pledged capital with respect to each respective capital lease agreement.

Future cash payments, including interest, under contractual obligations in effect as of December 31, 2001, are as follows:

Period	Term Loans	Operating Leases	Capital Leases	Total
		(In thousands)		
2002	$ 31	$ 502	$ 76	$ 609
2003	31	501	76	608
2004	31	480	76	587
2005	7	223	69	299
2006	—	139	47	186
Thereafter	—	475	—	475
Total contractual cash commitments	$100	$2,320	$344	$2,764

Related Party Transactions

The Company subcontracts a key portion of its final packaging processes to an independent third-party contract manufacturer. If such services were not available at a reasonable cost from our existing contract manufacturer, we would need to obtain new contracts with new providers or incur the expense of internalizing the packaging process. Such a conversion could cause us to incur additional expense in validating the process under FDA Good Manufacturing Practices, delay the availability of finished product and limit commercial sales of our products.

Receivable from related party represents the portion of offering expenses that Sepracor has agreed to pay as a result of Sepracor's participation in the July 2001 public offering of 4.0 million shares of our common stock. Total related party receivables are offset by amounts due to Sepracor for certain administrative services provided to us on an arms-length basis by Sepracor as of December 31, 2001. Total administrative fees charged for services rendered in the year ended December 31, 2001 were not material. All receivable from related party balances were received in full in February 2002.

Sepracor is entitled to certain rights with respect to the registration under the Securities Act of a total of 1,400,000 shares of our common stock. These rights provide that Sepracor may require us to register shares, subject to certain conditions and limitations. As of December 31, 2001, Sepracor has not exercised these rights.

As of December 31, 2001, the Company is not a party to any unconsolidated special purpose entity arrangements.

Recent Accounting Pronouncements

In 2002, Statement of Financial Accounting Standards or SFAS, No. 142, "Goodwill and Other Intangible Assets" became effective and as a result, we will cease to amortize $1.44 million of goodwill. During 2001, we recorded approximately $177,000 of amortization within selling, general and administrative expense and would have recorded an estimated $200,000 of amortization during 2002. In lieu of periodic amortization, we are required to perform an initial impairment review of our goodwill in 2002 and an annual impairment review thereafter. We expect to complete our initial review over the next six-month period.

We currently do not expect to record an impairment charge upon completion of the initial impairment review. However, there can be no assurance that at the time the review is completed a material impairment charge will not be recorded.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Derivative Financial Instruments, Other Financial Instruments, and Derivative Commodity Instruments

As of December 31, 2001, we did not participate in any derivative financial instruments or other financial and commodity instruments for which fair value disclosure would be required under Financial Accounting Standards Board Statement of Financial Accounting Standard No. 107 "*Disclosures About Fair Value of Financial Instruments.*"

Primary Market Risk Exposures

Our primary market risk exposures are in the area of foreign currency exchange rate risk. We are exposed to currency exchange rate fluctuations related to our operations in France. Operations in France are denominated in the euro. We have not engaged in formal currency hedging activities to date, but do have a limited natural hedge in that our expenses in France are primarily denominated in local currency, and we also attempt to minimize exchange rate risk by converting non-U.S. currency to U.S. dollars as often as practicable. We generally view

our investment in foreign subsidiaries with a functional currency other than our reporting currency as long-term. Our investment in foreign subsidiaries is sensitive to fluctuations in foreign currency exchange rates. The effect of a change in foreign exchange rates on our net investment in foreign subsidiaries is reflected in the "Other accumulated comprehensive loss" component of stockholders' equity. A ten-percent depreciation in year-end 2001 and 2000 functional currencies relative to the U.S. dollar would not result in a material reduction of stockholders' equity. Because our foreign currency exchange rate risk is not material, no quantitative tabular disclosure has been provided.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

REPORT OF INDEPENDENT ACCOUNTANTS

To the Board of Directors and Stockholders of BioSphere Medical, Inc. and subsidiaries:

We have audited the accompanying consolidated balance sheets of BioSphere Medical, Inc. (a Delaware Corporation) and subsidiaries as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' equity and comprehensive income (loss) and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of BioSphere Medical, Inc. and subsidiaries as of December 31, 2001 and 2000, and the results of their operations and their cash flows for the three years in the period ended December 31, 2001 in conformity with accounting principles generally accepted in the United States.

/s/ ARTHUR ANDERSEN LLP

Boston, Massachusetts
January 17, 2002.

BIOSPHERE MEDICAL, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands except share and per share amounts)

	December 31, 2001	December 31, 2000
ASSETS		
Current assets:		
Cash and cash equivalents	$ 10,569	$ 15,276
Marketable securities	12,550	—
Accounts receivable, net of allowance for doubtful accounts of $105 and $29 as of December 31, 2001 and 2000, respectively	1,809	1,142
Inventories, net	1,111	639
Receivable from related party	276	—
Prepaid and other current assets	282	124
Total current assets	26,597	17,181
Property and equipment, net	1,570	694
Goodwill, net	1,443	1,144
Other assets	374	287
Total assets	$ 29,984	$ 19,306
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 771	$ 924
Accrued compensation	1,383	994
Other accrued expenses	1,569	1,086
Payable to related party	—	14
Current portion of long-term debt and capital lease obligations	85	27
Total current liabilities	3,808	3,045
Minority interest acquisition obligation	—	478
Long-term debt and capital lease obligations	303	97
Total liabilities	4,111	3,620
Commitments (Note I)		
Stockholders' equity:		
Preferred stock, $0.01 par value, 1,000,000 shares authorized	—	—
Common stock, $0.01 par value, 25,000,000 shares authorized; 12,721,000 and 10,595,000 shares issued and outstanding as of December 31, 2001 and 2000, respectively	127	106
Additional paid-in capital	80,583	60,100
Accumulated deficit	(54,860)	(44,515)
Accumulated other comprehensive income (loss)	23	(5)
Total stockholders' equity	25,873	15,686
Total liabilities and stockholders' equity	$ 29,984	$ 19,306

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

BIOSPHERE MEDICAL, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)

	For the Years Ended December 31,		
	2001	2000	1999
Revenues:			
Product sales	$ 8,752	$ 3,961	$ 2,266
Collaboration revenue	250	—	—
Total revenue	9,002	3,961	2,266
Costs and expenses:			
Costs of product sales	2,356	1,461	1,404
Research and development	4,755	2,517	968
Selling, general and administrative (1)	12,839	7,847	4,003
Stock-based compensation to non-employees	—	1,261	—
Total costs and expenses	19,950	13,086	6,375
Loss from operations	(10,948)	(9,125)	(4,109)
Interest income	794	715	234
Interest expense	(31)	(54)	(134)
Other (expense) / income, net	(160)	17	15
Loss from continuing operations	(10,345)	(8,447)	(3,994)
Loss from discontinued operations	—	—	(539)
Net loss	$(10,345)	$ (8,447)	$(4,533)
Basic and diluted net loss per common share:			
Continuing operations	$ (0.89)	$ (0.87)	$ (0.47)
Discontinued operations	—	—	(0.06)
Total	$ (0.89)	$ (0.87)	$ (0.53)
Basic and diluted weighted average number of common shares outstanding	11,642	9,700	8,456

(1) Excludes compensation charges relating to the issuance of stock options to non-employees.

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

BIOSPHERE MEDICAL, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY AND COMPREHENSIVE INCOME (LOSS)
(In thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 1998	8,456	$ 84	$40,587	$(31,535)	$ —	$ 9,136
Comprehensive loss:						
Net loss	—	—	—	(4,533)	—	(4,533)
Translation adjustment	—	—	—	—	(15)	(15)
Total comprehensive loss	—	—	—	—	—	(4,548)
Balance at December 31, 1999	8,456	84	40,587	(36,068)	(15)	4,588
Comprehensive loss:						
Net loss	—	—	—	(8,447)	—	(8,447)
Translation adjustment	—	—	—	—	10	10
Total comprehensive loss						(8,437)
Issuance of common stock, net (Note L)	1,869	19	17,697	—	—	17,716
Issuance of common stock under employee benefit and incentive plans	270	3	555	—	—	558
Stock-based compensation to non-employee	—	—	1,261	—	—	1,261
Balance at December 31, 2000	10,595	106	60,100	(44,515)	(5)	15,686
Comprehensive loss:						
Net loss	—	—	—	(10,345)	—	(10,345)
Translation adjustment	—	—	—	—	28	28
Total comprehensive loss						(10,317)
Issuance of common stock, net (Note L)	2,000	20	20,334	—	—	20,354
Issuance of common stock under employee benefit and incentive plans	126	1	149	—	—	150
Balance at December 31, 2001	12,721	$127	$80,583	$(54,860)	$ 23	$ 25,873

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

BIOSPHERE MEDICAL, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	For the Years Ended December 31,		
	2001	2000	1999
Cash flows from operating activities:			
Net loss	$(10,345)	$ (8,447)	$(4,533)
Less: Net loss from discontinued operations	—	—	(539)
Net loss from continuing operations	(10,345)	(8,447)	(3,994)
Adjustments to reconcile net loss from continuing operations to net cash used in operating activities:			
Provision for doubtful accounts	83	37	—
Depreciation and amortization	523	279	102
Non-cash interest on minority interest obligation	—	19	—
Foreign exchange gain	—	(85)	—
Non-cash stock-based compensation for non-employees	—	1,261	—
Changes in operating assets and liabilities:			
Accounts receivable	(787)	(615)	121
Inventories	(527)	(250)	5
Prepaid and other current assets	(254)	(271)	4
Related party receivable / payable	(289)	(54)	(362)
Accounts payable	(233)	308	103
Accrued compensation and other expenses	1,056	801	282
Net cash used in operating activities	(10,773)	(7,017)	(3,739)
Cash flows from investing activities:			
Purchase of property and equipment	(1,245)	(533)	(382)
Purchase of marketable securities	(12,550)	—	—
Cash paid for step acquisitions of Biosphere Medical, S.A.	(953)	(950)	—
Increase in other assets	—	—	(1)
Cash acquired through acquisition of 51% of Biosphere Medical, S.A.	—	—	283
Net cash used in investing activities	(14,748)	(1,483)	(100)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net	20,354	17,716	—
Proceeds from stock options exercised	150	558	—
Net repayments under line of credit agreements	—	—	(2,000)
Net proceeds (payments) on long-term debt and capital leases	271	124	(664)
Net cash provided by (used in) financing activities	20,775	18,398	(2,664)
Effect of exchange rate changes on cash and cash equivalents	39	10	(7)
Net (decrease) increase in cash and cash equivalents	(4,707)	9,908	(6,510)
Net cash provided by discontinued operations	—	—	9,643
Cash and cash equivalents at beginning of year	15,276	5,368	2,235
Cash and cash equivalents at end of year	$ 10,569	$15,276	$ 5,368
Supplemental disclosure of cash flows information:			
Cash paid for interest	$ 8	$ 5	$ 134
Supplemental disclosure of non-cash investing activities (note C):			
Acquisition of Biosphere Medical, SA:			
Fair value of assets acquired	$ —	$ —	$ 1,493
Liabilities assumed	—	—	(1,493)
Minority interest acquisition obligation	—	188	771
Goodwill	$ —	$ 188	$ 771

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

A – Nature of the Business

BioSphere Medical, Inc ("we," "BioSphere" or the "Company") was incorporated in Delaware in December 1993 under the name BioSepra Inc. During 1999, the Company strategically refocused its business on the development and commercialization of its proprietary Embosphere Microspheres for use in treating hypervascularized tumors and malformations. Between February 1999 and October 2001 we acquired all ownership interests in Biosphere Medical S.A. ("BMSA"), a French société anonyme (See Note C). BMSA holds the license to the embolotherapy device that is the main focus of our business. In May 1999, we sold substantially all of our assets relating to our former core business, chromatography, and changed our name to BioSphere Medical, Inc. On July 3, 2001, we completed an underwritten public offering of 4.0 million shares of our common stock. Of the 4.0 million shares of our common stock offered, the Company sold 2.0 million shares and Sepracor Inc., a selling stockholder, sold 2.0 million shares. Net proceeds to the Company were approximately $20.4 million. On August 6, 2001, Sepracor sold an additional 600,000 shares of our common stock pursuant to exercise of the underwriter's over-allotment option. As a result of this offering, including the sale of shares associated with the over-allotment option, Sepracor's beneficial ownership interest in our outstanding common stock decreased from approximately 55% to approximately 25% (See Note D and L).

During 2000, the Company established two wholly owned subsidiaries to pursue the development of other microsphere applications and technologies. In May 2000, BioSphere Medical Japan, Inc., a Delaware corporation, was established to develop and commercialize Embosphere Microspheres as well as HepaSphere SAP Microspheres in Asia. In December 2000, BSMD Ventures, Inc., also a Delaware corporation, was established to explore and develop alternative applications for the Company's microsphere platform technology with a specific focus on dermal and other tissue engineering uses.

The Company believes that current working capital along with anticipated sales of its EmboSphere Microspheres and other products, will provide liquidity sufficient to allow the Company to meet its expected spending obligations for the foreseeable future while also allowing the further development and testing of other product candidates and technologies. However, no assurances can be given that such revenues will, in fact, be realized. Should the Company not realize some or all of its revenue projections, it may be required to secure alternative financing arrangements, pursue additional strategic partners, and/or defer or limit some or all of its research, development and/or clinical projects.

B – Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries BMSA, Biosphere Medical Japan, Inc. and BSMD Ventures, Inc. All material intercompany balances and transactions have been eliminated in consolidation.

Translation of Foreign Currencies

The assets and liabilities of the Company's foreign subsidiaries is translated into U.S. dollars using the exchange rates in effect as of each balance sheet date. Revenue and expense items are translated at average exchange rates prevailing during each reporting period. Resulting translation adjustments are recorded in the cumulative translation adjustment account in stockholders' equity. Aggregate foreign exchange transaction gains and losses are not material and are included in other income in the accompanying statement of operations for all periods presented.

B – Summary of Significant Accounting Policies (Continued)

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the following: (1) the reported amounts of assets and liabilities, (2) the disclosure of contingent assets and liabilities at the date of the financial statements and (3) the reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

Cash, Cash Equivalents and Marketable Securities

The Company considers all highly liquid investments with an original maturity of ninety days or less, as of the date of purchase, to be cash equivalents.

In accordance with our investment policies, surplus cash is invested in investment grade corporate and government debt and asset backed securities typically with maturity dates of less than 180 days. The Company determines the appropriate classification of marketable securities at each balance sheet date. Marketable securities as of December 31, 2001, classified as held to maturity for which we have the positive intent and ability to hold to maturity, are reported at amortized cost, which approximates fair market value.

Concentration of Credit Risk and Off-Balance Sheet Risk

The Company has no significant off-balance-sheet risk or concentration of credit risk such as foreign exchange contracts, option contracts or other foreign hedging arrangements. Financial instruments that potentially subject the Company to concentration of credit risk consist primarily of cash, cash equivalents, marketable securities, amounts due from related parties, trade accounts receivable, accounts payable and long-term debt obligations. The estimated fair value of the Company's financial instruments approximate their carrying value. BioSphere Medical places its cash, cash equivalents and marketable securities with high credit quality financial institutions. Concentrations of credit risk with respect to trade accounts receivable are limited due to a large number of customers and their dispersion across many geographic areas.

The Company subcontracts a key portion of its final packaging processes to an independent third-party contract manufacturer. If such services were not available at a reasonable cost from the existing contract manufacturer, we would need to obtain new contracts with new providers or incur the expense of internalizing the packaging process. Such a conversion could cause the Company to incur additional expense in validating the process under FDA Good Manufacturing Practices, delay the availability of finished product and limit commercial sales of our products.

Property and Equipment

Property and equipment are stated at cost. The Company provides for depreciation based upon expected useful lives using the straight-line method over the following estimated useful lives:

Office equipment	3-5 years
Laboratory and manufacturing equipment	3-5 years
Leasehold improvements	Shorter of lease term or estimated useful life

Maintenance and repairs are charged to expense as incurred. Upon retirement or sale, the cost of disposed assets and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to non-operating income.

B – Summary of Significant Accounting Policies (Continued)

Goodwill and Other Assets

Goodwill represents the difference between the purchase price and the fair value of the tangible and identifiable intangible net assets acquired in accordance with the purchase method of accounting. Between February 1999 and October 2001, the Company recorded goodwill upon the periodic step-acquisitions of additional interests of BMSA. Goodwill is amortized over the shorter of an estimated ten-year useful life or February 2009, which represents a ten-year amortization period from the date of the original BMSA purchase agreement (See Note C). Accumulated amortization was approximately $351,000 and $174,000 as of December 31, 2001 and December 31, 2000, respectively.

Impairment of Long-Lived Assets

As of December 31, 2001, the Company has evaluated the potential impairment of its long-lived assets with respect to events or changes in circumstances that may indicate that the carrying amount of a recorded asset may not be recoverable. Based on management's assessment as of December 31, 2001, the Company has determined that no impairment of long-lived assets exists.

Revenue Recognition

Revenues from product sales are recognized when requested goods are shipped to customers and collectibility is probable. Management establishes reserves for potential sales returns and evaluates, on a monthly basis, the adequacy of those reserves based upon realized experience. To date, returns have been minimal and immaterial. The Company adopted the Security and Exchange Commission's Staff Accounting Bulletin No. 101, *Revenue Recognition,* in the year ended December 31, 2000, with no material impact to the Company's results of operations.

Research and Development

Research and development costs are expensed in the period incurred.

Income Taxes

The Company uses the asset and liability accounting method whereby deferred tax assets and liabilities are recognized based on temporary differences between the financial statements and tax bases of assets and liabilities using current statutory tax rates. A valuation allowance against net deferred tax assets is recorded if, based on the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Management evaluates, on a quarterly basis, the ability to recover the deferred tax assets and the level of the valuation allowance. At such time as it is more likely than not that deferred tax assets are realizable, the valuation allowance will be appropriately reduced.

Comprehensive Income /(Loss)

Comprehensive income/(loss) is comprised of net income/(loss) and other comprehensive income/(loss). Other comprehensive income/(loss) includes certain changes in equity that are excluded from net income/(loss). Specifically, the effects of foreign currency translation adjustments which are reflected separately in stockholders' equity, are included in accumulated other comprehensive income/(loss).

B – Summary of Significant Accounting Policies (Continued)

Net Loss Per Share

Basic net loss per share is calculated based on the weighted average number of common shares outstanding during the period. Diluted net loss per share incorporates any dilutive effects of common stock equivalent options, warrants and other convertible securities. Total warrants and options potentially convertible into common stock as of December 31, 2001, 2000 and 1999, equaled 4,086,000, 4,147,000 and 3,783,000, respectively. All common stock equivalents have been excluded from the calculation of weighted average number of diluted common shares, as their effect would be antidilutive for all periods presented.

New Accounting Pronouncements

In June 2001, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards (SFAS) No. 141, "*Business Combinations.*" SFAS 141 requires all business combinations initiated after June 30, 2001 to be accounted for using the purchase method. Adoption of this statement did not have a material impact on the Company's operations.

In June 2001, the FASB issued SFAS No. 142, "*Goodwill and Other Intangible Assets.*" With the adoption of SFAS No. 142, goodwill and certain intangible assets with identifiable lives will no longer be subject to amortization over its estimated useful life, but instead goodwill is subject to at least an annual valuation and assessment for impairment by applying a fair-value-based test. Adoption of this statement is not expected to have a material impact on operations other than to exclude an estimated $201,000 in goodwill amortization from selling, general and administrative expenses in each respective year through 2008.

In June 2001, the FASB issued SFAS No. 143, "*Accounting for Asset Retirement Obligations.*" This statement addresses financial accounting and reporting for obligations associated with the retirement of tangible long-lived assets and the associated asset retirement costs. It applies to legal obligations associated with the retirement of long-lived assets that result from the acquisition, construction, development and (or) the normal operation of a long-lived asset, except for certain obligations of lessees. This statement amends FASB Statement No. 19 and is effective for financial statements issued for fiscal years beginning after June 15, 2002. The Company does not expect the adoption of this statement to have a material impact on its operations.

In August 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets." This statement supercedes SFAS Statement No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," and the accounting and reporting provisions of Accounting Principles Board Opinion No. 30, "Reporting the Results of Operations – Reporting the Effects of Disposal of a Segment of a Business, and Extraordinary, Unusual and Infrequently Occurring Events and Transactions." This statement requires that one accounting model be used for long-lived assets to be disposed of by sale, whether previously held and used or newly acquired, and it broadens the presentation of discontinued operations to include more disposal transactions. The provisions of this statement are effective for financial statements issued for fiscal years beginning after December 15, 2001, and interim periods within those fiscal years, with early adoption permitted. The Company does not expect the adoption of this statement to have a material impact on its operations.

C – Step Acquisition of Biosphere Medical S.A. and Minority Interest Acquisition Obligation

On February 25, 1999, the Company acquired 51% of the outstanding capital stock of BMSA. Pursuant to a February 25, 1999 purchase agreement, the Company acquired a this ownership interest by granting to BMSA an exclusive sales and manufacturing license to certain patents and technology primarily relating to the Company's

C – Step Acquisition of Biosphere Medical S.A. and Minority Interest Acquisition Obligation (Continued)

Embosphere Microspheres technology. The Company was also granted an option to purchase the remaining 49% interest in BMSA through December 31, 2004, for an amount equal to the product of the percentage interest to be purchased and the sum of BMSA's rolling average twelve-month sales and worldwide Embosphere Microspheres sales as of the date of exercise (the "Purchase Option"). Moreover, the holder of the remaining 49% interest was also granted an option (the "Put Option") to require the Company to purchase the remaining 49% interest from December 31, 2003 until December 31, 2004 for an amount equal to the greater of an agreed upon price (in French Francs) for each percentage interest to be sold or the amount payable adjusted to a rolling nine-month sales average under the Purchase Option. The Put Option represented a contingent purchase consideration for which the Company accreted the value of the Put Option through October 31, 2001.

On April 7, 2000, the Company purchased an additional 34% of BMSA for $950,000. As a result of this step-acquisition, the Company's total ownership interest in BMSA increased to 85%. On November 5, 2001, the Company acquired the remaining 15% interest in BMSA for approximately $953,000. Both subsequent step-acquisition transactions were accounted for under purchase accounting principles whereby the fair value in excess of the net assets purchased is treated as an increase to goodwill. Net goodwill, comprised entirely of the unamortized purchase price paid in excess of the net BMSA assets acquired, equaled $1.4 million and $1.1 million as of December 31, 2001 and December 31, 2000, respectively.

D – Related Party Transactions

Receivable from related party at December 31, 2001 represents the portion of expenses that Sepracor has agreed to pay as a result of Sepracor's participation in the July 2001 secondary offering of 4.0 million shares of the Company's common stock. Total related party receivables are offset by $83,000 due to Sepracor for certain administrative services provided by Sepracor as of December 31, 2001. Total administration fees, including rent through April 2000, charged by Sepracor for services rendered in the years ended December 31, 2001, 2000 and 1999 were $20,000, $111,000 and $119,000, respectively.

Sepracor is also entitled to certain rights with respect to the registration under the Securities Act of a total of 1,400,000 shares of BioSphere's Common Stock. These rights provide that Sepracor may require BioSphere Medical to register shares, subject to certain conditions and limitations. As of December 31, 2001, Sepracor has not exercised such rights.

E – Marketable Securities

Cash and cash equivalents include $10.2 million and $15.2 million of commercial paper and money market funds as of December 31, 2001 and 2000, respectively. The Company's cash, cash equivalents and marketable securities as of December 31, 2001 are as follows:

	December 31, 2001
	(in thousands)
Cash and money market funds	$ 7,569
Commercial paper	3,000
Asset-backed government securities	12,550
Total	23,119
Less amounts classified as cash and cash equivalents	(10,569)
Total marketable securities	$ 12,550

E – Marketable Securities (Continued)

As the maturity dates on all marketable securities held as of December 31, 2001 were less than 90 days, amortized cost approximates fair market value. No realized gains or losses on held to maturity securities were recognized during the twelve-month period ended December 31, 2001.

F – Inventories

Inventories are stated at the lower of cost (first-in, first-out) or market and consist of the following as of:

	December 31,	
	2001	2000
	(In thousands)	
Raw material	$ 185	$156
Work in progress	269	78
Finished goods	657	405
Total inventory	$1,111	$639

G – Property and Equipment

Property and equipment consists of the following as of:

	December 31,	
	2001	2000
	(In thousands)	
Office equipment	$ 827	$ 469
Laboratory and manufacturing equipment	1,056	425
Leasehold improvements	272	45
Total property and equipment	2,155	939
Less: accumulated depreciation	(585)	(245)
Net property and equipment	$1,570	$ 694

Depreciation expense was $341,000, $161,000 and $49,000 for the years ended December 31, 2001, 2000 and 1999, respectively.

H – Debt and Other Obligations

Debt consists of the following as of:

	December 31,	
	2001	2000
	(In thousands)	
5.4% French Franc term loan payable to a bank in monthly installments through March 2005, secured by the net assets of BMSA	$ 92	$124
Capital lease obligations (see note I)	296	—
Less: current portion	(85)	(27)
Total long-term debt and capital lease obligations	$303	$ 97

As a co-borrower under Sepracor's commercial bank facility, we had availability to borrow up to $2.0 million through a line of credit agreement. As a result of our July 2001 secondary public offering, Sepracor's ownership of our outstanding common stock was reduced to less than 50%, thereby automatically terminating the co-borrowing arrangement. Because we are no longer a party to the loan agreement, which had no outstanding balance as of December 31, 2001, the bank released Sepracor's guaranty of our obligations to the bank and Sepracor terminated its related security interest in our assets.

I – Commitments

The Company leases approximately 13,000 square feet of office and lab space at its Rockland facility under an operating lease expiring in February 2005 for approximately $139,000 per year.

BMSA leases approximately 18,150 square feet of manufacturing and office space in Roissy, France through December 2009 for approximately €157,000 per year (approximately $139,000 as of December 31, 2001). BMSA also has several operating leases covering certain pieces of manufacturing and office equipment through March 2005.

During fiscal year 2001, the Company entered into several non-cancelable capital lease agreements in connection with the acquisition of certain manufacturing and computer equipment. The leases have initial terms of 30 to 60 months with interest rates of 5.4% to 13.4%. All corresponding leased equipment serves as pledged capital.

Future minimum lease payments under non-cancellable operating leases and capital leases in effect as of December 31, 2001, are as follows:

Period	Operating Leases	Capital Leases
	(In thousands)	
2002	$ 502	$ 76
2003	501	76
2004	480	76
2005	223	69
2006	139	47
Thereafter	475	—
Total lease commitments	$2,320	$344
Less amount representing interest		(48)
Present value of net minimum capital lease payments		$296

Total rental expense for the years ended December 31, 2001, 2000 and 1999 was approximately $464,000, $245,000 and $81,000, respectively.

J – Income Taxes

As of December 31, 2001, the Company had federal and state net operating loss (NOL) carryforwards of approximately $43.6 million, which will expire through the year 2021. As of December 31, 2001, research and experimentation credit carryforwards approximated $281,000, which will expire through the year 2015. The components of the Company's net deferred tax asset are as follows at:

	December 31,	
	2001	2000
	(In thousands)	
Assets		
Domestic NOL carryforwards	$ 14,813	$ 11,470
Tax credit carryforwards	281	281
Property and equipment	5	(44)
Other	755	138
Subtotal	15,854	11,845
Valuation allowance	(15,854)	(11,845)
Net deferred tax asset	$ —	$ —

J – Income Taxes (Continued)

The Company has established a full valuation allowance against its deferred tax asset as of December 31, 2001 as it considers the realizable value of any tax benefit against future taxable income to be uncertain.

K – Segment Information

The Company develops microspheres for use in the treatment of hypervascularized tumors and malformations. The Company operates exclusively in the medical device business, which the Company considers as one business segment. Financial information by geographic area is as follows:

	For the years ended December 31,		
	2001	2000	1999
	(In thousands)		
Revenue			
United States			
Unaffiliated customers	$ 6,018	$ 1,266	$ —
Licensing fees	250	—	—
France and other Europe territories			
Unaffiliated customers – (Primarily French)	2,324	2,183	1,949
Intercompany	3,504	1,405	—
Transfer to other geographic areas	410	512	317
	12,506	5,366	2,266
Intercompany eliminations	(3,504)	(1,405)	—
Total revenue	$ 9,002	$ 3,961	$ 2,266
Operating losses			
United States	$(11,561)	$(8,976)	$(3,965)
Europe	613	(149)	(144)
Total operating loss	$(10,948)	$(9,125)	$(4,109)

Long-lived assets as of December 31,	2001	2000
United States	$ 2,803	$ 2,241
Europe	904	412
Eliminations	(320)	(528)
Total long-lived assets	$ 3,387	$ 2,125

L – Capital Stock

Common Stock

The Company's authorized capital stock includes 25,000,000 shares of common stock, par value $0.01 per share. As of December 31, 2001, 3.22 million shares, or approximately 25%, of the Company's common stock outstanding is held by Sepracor. The common stock has no preemptive, subscription, redemption or conversion rights.

Preferred Stock

The Company's authorized capital stock includes 1,000,000 shares of preferred stock, par value $0.01 per share, with such rights, restrictions and specifications as the Board of Directors may determine. As of December 31, 2001 and 2000, no shares of preferred stock have been issued.

L – Capital Stock (Continued)

Common Stock Financing

In February 2000, the Company completed a private equity placement of common stock and warrants for net proceeds of approximately $5.9 million. Investors purchased 653,887 shares of the Company's common stock at a price of $9.00 per share, which included warrants to purchase up to an additional 163,468 shares of common stock. Of the total 653,887 common shares sold, unrelated third-party institutional investors purchased 609,445, or 93%, and 44,442, or 7%, were purchased by executive officers and members of the Company's Board of Directors. The warrants have an exercise price equal to $20.00 per share and expire on February 4, 2005. Using the Black-Scholes option-pricing model, the Company valued the warrants at approximately $929,000 and included such amount as a component of additional paid-in capital.

In July 2000, the Company completed an additional private equity placement of common stock for net proceeds of approximately $11.8 million. Investors purchased 1,214,900 shares of common stock at $11.00 per share. Of the total shares sold, Sepracor Inc., which was at the time of the private placement the Company's parent company, purchased 454,545 shares, after which its majority ownership decreased to 55%.

On July 3, 2001, the Company completed an underwritten public offering of 4.0 million shares of its common stock at $11.00 per share. Of the 4.0 million shares of common stock offered, the Company sold 2.0 million shares and Sepracor sold 2.0 million shares. Net proceeds to the Company were approximately $20.4 million. On August 6, 2001, Sepracor sold an additional 600,000 shares of our common stock pursuant to exercise of the underwriters' over-allotment option. As a result of this offering, including the sale of shares pursuant to exercise of the over-allotment, Sepracor's beneficial ownership interest in the Company's outstanding common stock decreased from approximately 55% to approximately 25% as of December 31, 2001.

M – Stock Plans and Warrants

Stock Option Plans

The 1994 stock option plan (the "1994 Plan") provides for the grant of both incentive stock options ("ISOs") and non-statutory stock options ("NSOs") to officers, directors, advisors and key employees of the Company. The 1994 Plan also provides for the grant of NSOs to consultants of the Company. The exercise price for ISOs must be at least equal to the fair market value of the Company's common stock on the date of grant and the exercise price of NSOs must be at least equal to 50% of the fair market value of the Company's common stock on the date of grant. Options generally become exercisable in five equal annual installments beginning on the first anniversary of the date of grant. ISOs have a maximum term of ten years from the date of grant. A total of 1.0 million shares were approved for issuance under the 1994 Plan and as of December 31, 2001, approximately 303,000 shares were available for issuance.

The Company's 1997 Stock Option Plan, as amended, (the "1997 Plan") provides for the grant of both ISOs and NSOs to officers, directors, advisors and key employees of the Company. The 1997 Plan also provides for the grant of NSOs to consultants of the Company. In September 2000, the Company's Board of Directors approved an amendment to the 1997 Stock Incentive Plan to increase the number of shares of common stock available for issue from 3,125,000 shares to 5,000,000 shares. As of December 31, 2001, approximately 1,582,000 shares under the 1997 plan were available for issuance. Options generally become exercisable in five equal annual installments beginning on the first anniversary of the date of grant.

M – Stock Plans and Warrants (Continued)

The Director Option Plan (the "Director Plan"), as amended, provides for the granting of NSOs to directors of the Company who are not officers or employees of the Company or of any subsidiary of the Company. A total of 300,000 shares of common stock may be issued under the Director Plan subject to adjustments as provided therein. The exercise price per share will equal the fair market value of a share of Company's common stock on the date on which the option is granted. Options granted under the Director Plan will vest in either two or five equal installments beginning on the first anniversary of the date of the grant depending on the nature of the grant. As of December 31, 2001, there were 116,000 options available for issuance under the Director Plan.

The following table summarizes all stock option activity under the three stock option plans for the three years ended December 31, 2001:

	Options issued under the Plans	
	Shares	Average Price Per Share
	(In thousands, except option price)	
Outstanding at December 31, 1998	1,582	$ 2.37
Granted	2,549	0.94
Canceled	(393)	2.15
Outstanding at December 31, 1999	3,738	$ 1.42
Granted	516	14.88
Exercised	(266)	2.09
Canceled	(44)	2.79
Outstanding at December 31, 2000	3,944	$ 3.12
Granted	200	12.19
Exercised	(122)	1.04
Canceled	(139)	16.29
Outstanding at December 31, 2001	3,883	$ 3.18

The following options and their respective average prices per share were outstanding and exercisable at December 31, 2001, 2000 and 1999:

	Outstanding	Average Price Per Share	Exercisable	Average Price Per Share
	(In thousands, except option price)			
December 31, 2001	3,883	$3.18	1,818	$2.85
December 31, 2000	3,944	3.12	1,147	2.11
December 31, 1999	3,738	1.42	1,016	2.39

M – Stock Plans and Warrants (Continued)

Options vest at various rates over periods of up to five years and may be exercised within ten years from the date of grant. The following table summarizes information about total stock options under the three plans, outstanding and exercisable as of December 31, 2001:

		Options Outstanding		Options Exercisable	
Range of Exercise Prices	Number Outstanding	Remaining Contractual Life (Years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
		(In thousands except per share amounts)			
$ 0.81 – 1.25	2,180	7.13	$ 0.84	634	$ 0.84
1.26 – 1.89	351	5.97	1.79	345	1.80
1.90 – 2.85	651	4.25	2.20	567	2.19
2.86 – 4.30	90	4.56	3.37	90	3.37
4.31 – 6.50	40	3.82	5.15	40	5.15
6.51 – 9.75	46	9.78	7.75	—	—
9.76 – 14.50	332	8.82	11.93	61	11.66
14.51 – 21.75	163	8.75	17.27	67	17.64
21.76 – 27.25	30	8.13	27.25	14	27.25
	3,883		$ 3.18	1,818	$ 2.85

The Company applies the principles of Accounting Principles Board Opinion No. 25, "*Accounting for Stock Issued to Employees*," and related interpretations in accounting for its Plans. Accordingly, no compensation expense has been recognized for its employee stock-based compensation plans. Had compensation costs for the Company's stock-based compensation been determined based on the fair value at the grant dates as calculated in accordance with SFAS No. 123, "*Accounting for Stock-Based Compensation*," the Company's reported net loss and net basic and diluted loss per common share for the years ended December 31, 2001, 2000 and 1999 would have been adjusted to the pro forma amounts indicated below:

	For the years ended December 31,		
	2001	2000	1999
	(In thousands, except per share amounts)		
Net Loss			
As reported	$(10,345)	$(8,447)	$(4,533)
Pro forma	(12,017)	(9,227)	(7,612)
Basic and diluted loss per share			
As reported	(0.89)	(0.87)	(0.53)
Pro forma	(1.03)	(0.95)	(0.90)

M – Stock Plans and Warrants (Continued)

The average fair value of options granted, $10.05, $12.39, and $0.82 for fiscal years 2001, 2000, and 1999, respectively, was estimated using the Black-Scholes option-pricing model using the following weighted-average assumptions:

	2001	2000	1999
Dividend Yield	None	None	None
Volatility	113%	110%	106%
Risk-free interest rate	4.0%–5.0%	5.5%–6.2%	4.9%–6.7%
Expected life (years)	5	5	7

The Black-Scholes option-pricing model was developed for use in estimating the fair value of traded options that have no vesting restrictions and are fully transferable. In addition, option-pricing models require the use of highly subjective assumptions, including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective assumptions can materially affect the fair value estimates, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock-based compensation.

Employee Stock Purchase Plans

Under the 1997 employee stock purchase plan (the "1997 ESPP"), an aggregate of 50,000 shares of common stock may be purchased by employees at 85% of the fair market value on the first or last day of each six month offering period, whichever is lower. An eligible employee may elect to have up to a maximum of 10% deducted through payroll deductions from his or her regular salary. During 2001, 2000 and 1999, there were 0, 0, and 4,876 shares of the Company's common stock, respectively, were issued under the 1997 ESPP.

In June 2000, stockholders approved the 2000 employee stock purchase plan (the "2000 ESPP") to replace the Company's 1997 Plan. Under the 2000 ESPP, an aggregate of 50,000 shares of common stock may be purchased by employees at 85% of the fair market value on the first or last day of each six month offering period, whichever is lower. During each offering period, the maximum number of shares which may be purchased by a participating employee is determined on the first day of the offering period and is equal to the number of shares of common stock determined by dividing $12,500 by the last reported sale price of the common stock on the Nasdaq National Market on the first day of the offering. An eligible employee may elect to have up to a maximum of 10% deducted through payroll deductions from his or her regular salary. During 2000, no shares were issued under the 2000 ESPP. During 2001, 3,683 shares of the Company's common stock were issued under the 2000 ESPP.

Stock-Based Compensation to Non-Employees

In connection with stock options previously issued to non-employees, the Company's Board of Directors authorized the Company to accelerate the vesting of all non-employee advisors' stock options subject to variable accounting principles. Accordingly, $1,261,000 in non-cash compensationexpensewas recorded and presented as a separate line item within the statement of operations for the year ended December 31, 2000. The recorded $1,261,000 aggregate fair value of the non-employee stock options was derived from the Black-Scholes option-pricing model.

Stock Warrants

In 1997, the Company issued a warrant to purchase 45,000 shares of the Company's common stock at $3.00 per share. The warrant expires on June 5, 2002. As of December 31, 2000, the warrant had vested with respect to 40,000 shares. The remaining 5,000 shares are not exercisable due to the failure of the holder to satisfy certain vesting requirements.

N – Employees Savings Plan

The Company has a 401(k) savings plan for all domestic employees pursuant to which eligible employees may voluntarily contribute up to 15% of their compensation subject to statutory limitations. In addition, the Company matches in cash 50% of the first $3,000 contributed by employees up to a $1,500 maximum per employee. Employer cash matching contributions amounted to approximately $44,000, $18,000, $11,000 for the years ended December 31, 2001, 2000 and 1999, respectively.

O – Discontinued Operations

On May 17, 1999, the Company sold substantially all of the assets of its business, for approximately $11.0 million ($9.6 million, net) in cash and the assumption of certain liabilities. Upon the consummation of the sale, BioSepra, Inc. changed its name to BioSphere Medical, Inc. The Company utilized a portion of the proceeds to pay approximately $880,000 of transaction costs, to repay approximately $2.0 million of outstanding bank debt, and to repay approximately $143,000 due to Sepracor.

The net assets included in the sale had a net book value of approximately $10.5 million on May 17, 1999, which was included in calculating a net loss on the sale of approximately $70,000. The operations of the business have been presented in accordance with disposal of a segment of a business and discontinued operations accounting principles in the accompanying consolidated financial statements. Accordingly, the operating results of the discontinued business for the year ended December 31, 1999 have been segregated from the continuing operations and reported as a separate line item on the consolidated statements of operations.

P – Valuation and Qualifying Accounts

The Company monitors the credit worthiness of its trade customers based upon historical payment experience. A rollforward of the allowance for doubtful accounts for the years ended December 31, 2001, 2000 and 1999 is as follows:

	Balance, Beginning of Period	Charged to Costs and Expenses	Deductions	Balance, End of Period
		(In thousands)		
Year ended December 31, 2001	$ 29	$83	$ (7)	$105
Year ended December 31, 2000	$ —	$37	$ (8)	$ 29
Year ended December 31, 1999	$106	—	$(106)	—

Q – Quarterly Financial Data (Unaudited)

The following is a summary of quarterly financial results:

	Fourth Quarter	Third Quarter	Second Quarter	First Quarter
	(In thousands except per share amounts)			
Net revenue				
2001	$ 2,725	$ 2,017	$ 2,413	$ 1,847
2000	1,356	1,016	815	774
Gross profit				
2001	2,024	1,470	1,824	1,328
2000	956	641	411	492
Net loss				
2001	(2,487)	(3,075)	(2,282)	(2,501)
2000	(2,371)	(2,453)	(2,147)	(1,476)
Diluted loss per share				
2001	(0.20)	(0.24)	(0.22)	(0.24)
2000	(0.23)	(0.24)	(0.23)	(0.17)

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

During 2001 and 2000, there were no disagreements with our independent accountants on accounting and financial disclosure matters.

PART III

Items 10–13.

The information required for Part III in this Annual Report on Form 10-K is incorporated by reference from the Company's definitive proxy statement for the Company's 2002 Annual Meeting of Stockholders. Such information will be contained in the sections of such proxy statement captioned "Stock Ownership of Certain Beneficial Owners and Management", "Election of Directors", "Board and Committee Meetings", "Compensation for Directors", "Compensation of Executive Officers", "Compliance with Section 16 Reporting Requirements", and "Certain Relationships and Related Transactions". Information regarding executive officers of the Company is also furnished in Part I of this Annual Report on Form 10-K under the heading "Executive Officers."

PART IV

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

(a) The following documents are included as part of this Annual Report on Form 10-K.

1. The Schedule listed below and the Reports of Independent Accountants on financial statement schedules are filed as part of this Annual Report on Form 10-K.

   All other schedules are omitted as the information required is inapplicable or the information is presented in the consolidated financial statements or the related notes.

2. The Exhibits listed in the Exhibit Index immediately preceding the Exhibits are filed as a part of this Annual Report on Form 10-K.

(b) Current Reports on Form 8-K filed during the last quarter of the fiscal year.

On December 7, 2001, the Company filed a report on Form 8-K to report, pursuant to Item 5, that the Company had issued a press release on November 29, 2001 announcing the resignation of Jean-Marie Vogel as a director and as chairman of the Board of Directors and the acquisition of an outstanding minority interest in Biosphere Medical S.A.

Exhibit Index

Exhibit No.	Description
3.1	Certificate of Incorporation, as amended, of the Company. (Incorporated herein by reference to the Company's Registration Statement on Form S-8. (File No. 333-83639))
3.2	By-Laws of the Company. (Incorporated herein by reference to the Company's Registration Statement on Form S-1, as amended (File No. 33-75212)).
4	Specimen Certificate for shares of Common Stock, $.01 par value, of the Company. (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.1(1)	1994 Director Option Plan. (Incorporated herein by reference to the Company's Registration Statement on Form S-1, as amended (File No. 33-75212))
10.2	Form of Technology Transfer and License Agreement dated as of January 1, 1994 between the Company and Sepracor Inc. (Incorporated herein by reference to the Company's Registration Statement on Form S–1, as amended (File No. 33-75212))
10.3	Share Purchase Agreement by and between Marie-Paula Leroy-Landercy and the Company dated December 31, 1998. (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.4+	Joint Ownership Contract between the Company and L'Assistance Publique Hopitaux de Paris dated January 5, 1998, together with amendment dated February 10, 2000 (translated from French). (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.5*	Rider No. 2 dated June 20, 2000 to the Joint Ownership Contract between the Company and L'Assistance Publique Hopitaux de Paris dated January 5, 1998.
10.6+*	Exclusive License Agreement between Dr. Shin-ichi Hori and the Company dated May 8, 2000.
10.7+	Exclusive License and Know How Agreement No. L99037 by and between Le Centre National de la Recherche Scientifique, L'Universite Louis Pasteur Strasbourg and the Company dated July 15, 1999 (translated from French). (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.8	Form of Stock and Warrant Purchase Agreement dated as of February 4, 2000, between the Company (together with schedule of purchasers thereto). (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.9	Form of Warrant Agreement dated as of February 4, 2000, between the Company and certain purchasers (together with schedule of purchasers thereto). (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.10	Sublease Agreement between Guerbet S.A. and BiosphereMedical, S.A. (translated from French to English). (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.11	Lease Agreement dated January 7, 2000 by and between 1050 Hingham Street Realty Trust and the Company. (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.12	First Amendment to Lease Agreement dated June 27, 2000 by and between 1050 Hingham Street Realty Trust and the Company. (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 1999)
10.13	Stock Purchase Agreement dated July 28, 2000. (Incorporated herein by reference to the Company's Form 10-Q for the quarter ended June 30, 2000)

Exhibit No.	Description
10.14	Registration Rights Agreement dated July 28, 2000. (Incorporated herein by reference to the Company's Form 10-Q for the quarter ended June 30, 2000)
10.15	Lease Agreement dated October 19, 2000 by and between Biosphere Medical S.A. and Salamandre S.A (translated from French to English). (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 2000)
10.16+*	Exclusive Distribution Agreement dated January 24, 2002 by and between BioSphere Medical S.A. and Terumo Europe NV/SA, as amended on January 28, 2002.
21	Subsidiaries of the Company. (Incorporated herein by reference to the Company's Form 10-K for the year ended December 31, 2000)
23*	Consent of Arthur Andersen LLP.
99*	Letter to Commission Pursuant to Temporary Note 3T – Confirmation of Arthur Andersen Representations

(1) Management contract or compensatory plan or arrangement filed as an exhibit to this Form 10-K pursuant to Items 14(a) and 14(c) of Form 10-K.

\+ Confidential treatment requested as to certain portions.

* Filed herewith.

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.

BIOSPHERE MEDICAL, INC.

By: /s/ JOHN M. CARNUCCIO
John M. Carnuccio
President and Chief Executive Officer

Date: March 28, 2002

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ JOHN M. CARNUCCIO John M. Carnuccio	President, Chief Executive Officer, Director (Principal Executive Officer)	March 28, 2001
/s/ ROBERT M. PALLADINO Robert M. Palladino	Chief Financial Officer (Principal Financial and Accounting Officer)	March 28, 2001
/s/ TIMOTHY J. BARBERICH Timothy J. Barberich	Director	March 28, 2001
/s/ WILLIAM M. COUSINS, JR. William M. Cousins, Jr.	Director	March 28, 2001
_____ Alexander M. Klibanov, Ph.D.	Director	
/s/ PAUL A. LOONEY Paul A. Looney	Director	March 28, 2001
/s/ RICCARDO PIGLIUCCI Riccardo Pigliucci	Director	March 28, 2001
/s/ DAVID P. SOUTHWELL David P. Southwell	Director	March 28, 2001

BioSphere Medical Corporate Information

OFFICERS

John M. Carnuccio
President and Chief Executive Officer

Thomas M. Keenan
Vice President,
International Sales and Marketing

Jonathan R. McGrath
Vice President,
Worldwide Research and Development

Michael F. Miley
Vice President, U.S. Marketing

Robert M. Palladino
Vice President and
Chief Financial Officer

Robert T. Phelps
Vice President, U.S. Sales

BOARD OF DIRECTORS

Timothy J. Barberich
Chairman and Chief Executive Officer
Sepracor Inc.

John M. Carnuccio
President and Chief Executive Officer
BioSphere Medical, Inc.

William M. Cousins, Jr.
President, William M. Cousins, Jr., Inc.

Alexander M. Klibanov, Ph.D.
Professor of Chemistry
Massachusetts Institute of Technology

Paul A. Looney
President and Chief Operating Officer
Biopure Corporation

Riccardo Pigliucci
President and Chief Executive Officer
Discovery Partners International

David P. Southwell
Executive Vice President
and Chief Financial Officer
Sepracor Inc.

CORPORATE HEADQUARTERS

BioSphere Medical, Inc.
1050 Hingham Street
Rockland, MA 02370
North America
Tel: 800-394-0295
European Tel: +33.1.48.17.25.25
www.biospheremed.com

MARKET FOR COMMON STOCK

The Common Stock of BioSphere Medical, Inc. is traded on the Nasdaq Stock Market under the symbol BSMD.

TRANSFER AGENT AND REGISTRAR

American Stock Transfer and Trust Company
40 Wall Street
New York, NY 10005
212-936-5100

GENERAL COUNSEL

Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
617-526-6000

AUDITORS

Ernst & Young LLP
200 Clarendon Street
Boston, Massachusetts 02116
617-266-2000

BioSphere Medical Management Team. Pictured left to right, Jonathan R. McGrath, Robert M. Palladino, Michael F. Miley, John M. Carnuccio, Robert T. Phelps, and Thomas M. Keenan

ANNUAL MEETING

The Annual Meeting of Stockholders will be held at 12 PM on May 22, 2002, at Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109

TRADEMARKS

www.biospheremed.com

BioSphere Medical, Inc.
1050 Hingham Street
Rockland, MA 02370

Tel: 781.681.7900
Fax: 781.681.5093

Email: info@biospheremed.com