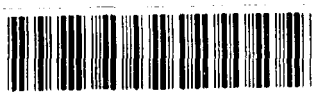

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K ARLS

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

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

For the fiscal year ended December 31, 2003

APR 30 2004

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 000-50405

Acusphere, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**04-3208947**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification No.)*
500 Arsenal Street Watertown, Massachusetts *(Address of principal executive offices)*	**02472** *(Zip Code)*

Registrant's telephone number, including area code: (617) 648-8800

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. ☑

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

The aggregate market value of Common Stock held by non-affiliates of the registrant as of March 16, 2004 (based on the last reported sale price on The Nasdaq National Market as of such date) was $73,962,997. As of March 1, 2004 there were 14,297,280 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this report incorporates information by reference from the Company's definitive proxy statement, which proxy statement is due to be filed with the Securities and Exchange Commission not later than 120 days after December 31, 2003.

INTRODUCTORY NOTE

This report, including the documents incorporated by reference in this report, includes statements that are not historical facts, which statements we refer to as "forward-looking statements". We have based these forward-looking statements on our current expectations and projections about future events. Forward-looking statements involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. In this Annual Report on Form 10-K, words such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements in these documents include, but are not limited to, those relating to:

- our plans to develop and market new products and the timing of these development programs, in particular the timing of clinical trials and regulatory milestones for AI-700;
- our clinical development of product candidates, clinical trials and our ability to obtain and maintain regulatory approval for our product candidates;
- our estimates regarding our capital requirements and our needs for additional financing;
- our estimates of expenses and future revenues and profitability;
- our estimates of the size of the potential markets for our product candidates; our selection and licensing of product candidates;
- our ability to attract collaborators with acceptable development, regulatory and commercialization expertise;
- the benefits to be derived from corporate collaborations, license agreements and other collaborative efforts, including those relating to the development and commercialization of our product candidates;
- sources of revenues and anticipated revenues, including contributions from corporate collaborations, license agreements and other collaborative efforts for the development and commercialization of products;
- our ability to create an effective direct sales and marketing infrastructure for products we elect to market and sell directly;
- the rate and degree of market acceptance of our product candidates;
- the timing and amount of reimbursement for our product candidates;
- the success of other competing therapies that may become available; and
- the manufacturing capacity for our product candidates.

Our actual results and the timing of certain events may differ materially from the results discussed, projected, anticipated or indicated in any forward-looking statement. Any forward-looking statement should be considered in light of factors discussed in Item 7 under "Certain Factors Which May Affect Future Results" and elsewhere in this Annual Report on Form 10-K. We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, to publicly update or revise any such statements to reflect any change in company expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

PART I

Item 1. *Business*

General

We are a specialty pharmaceutical company that develops new drugs and improved formulations of existing drugs using our proprietary porous microparticle technology. We are focused on developing proprietary drugs that can offer significant benefits over existing drugs, including improved safety and efficacy, increased patient compliance, greater ease of use, expanded indications or reduced cost. Our three product candidates are in clinical development and are designed to address large unmet clinical needs in the areas of cardiology, oncology and asthma. Our lead product candidate is an ultrasound contrast agent in Phase III clinical development for the detection of coronary artery disease, the leading cause of death in the United States.

Our proprietary technology enables us to control the size and porosity of particles, including nanoparticles and microparticles, in a versatile manner, so that we can customize the particles to address the delivery needs of a variety of drugs. We have initially applied this technology in our research and development efforts in the following areas:

- *AI-700, Intravenous Delivery of Gas for Ultrasound Contrast.* We specifically designed AI-700 to assess myocardial perfusion, or blood flow in the heart muscle, a sensitive marker for coronary artery disease. AI-700 is an ultrasound contrast agent that enables stress echocardiography, or ultrasound of the heart, to obtain information on myocardial perfusion. Currently, there is no ultrasound contrast agent that is approved by the U.S. Food and Drug Administration, or FDA, to assess myocardial perfusion. We initiated the Phase III clinical program for AI-700 in early 2003 with the pivotal phase of this program initiated at selected sites in late 2003.
- *AI-850, First Clinical-Stage Product Candidate from our Hydrophobic Drug Delivery System, HDDS.* Hydrophobic drugs, which are drugs that do not dissolve well in water, are often difficult to formulate, especially for intravenous delivery. We have demonstrated that our Hydrophobic Drug Delivery System, or HDDS, improves the dissolution rate of a variety of hydrophobic drugs. Our first clinical application of HDDS is AI-850, which is in Phase I clinical trials. AI-850 is an improved formulation of paclitaxel, the active ingredient in Taxol, a leading cancer drug.
- *AI-128, First Clinical-Stage Product Candidate from our Pulmonary Drug Delivery System, PDDS.* Most asthma drugs delivered via inhalation are immediate release formulations that must be inhaled multiple times per day, reducing patient compliance. We have completed a Phase I study for AI-128, a sustained release formulation of an FDA-approved asthma drug.

Our Porous Microparticle Technology

Microparticles are useful in the delivery of a wide range of drugs. The suitability of microparticles for use in drug delivery depends on a variety of characteristics, including size and porosity. We created our three initial product candidates using technology that enables us to control the size and porosity of nanoparticles and microparticles in a versatile manner so that we can customize the particles to address the delivery needs of a variety of drugs. We are focused on creating porous particles that are smaller than red blood cells. These microparticles can be used to deliver gases or these microparticles and nanoparticles can be used to deliver drugs to patients through various routes of delivery. Small microparticles are important for delivering drugs intravenously so that they can pass safely through the body's smallest blood vessels, for increasing the surface area of a drug so that it will dissolve more rapidly, and for delivering drugs via inhalation. Porosity is important for entrapping gases in microparticles, for controlling the release rate of the drug from a microparticle, and for targeting inhaled drugs to specific regions of the lung. Our porous microparticle technology enables us to produce microparticles that are smaller than red blood cells, with a wide range of porosities. We have developed proprietary spray drying equipment and pore forming processes that enable us to produce these porous microparticles in a versatile manner.

Using our proprietary technology:

- We have produced small, hollow microparticles, which are analogous in structure to ping pong balls, containing gas. Using these microparticles, we are developing AI-700, an ultrasound contrast agent for detection of coronary artery disease through the assessment of myocardial perfusion.
- We have produced small microparticles with tiny pores throughout, which are analogous in structure to sponges. Using these microparticles, we are developing our HDDS technology, which may enable the dissolution of hydrophobic drugs in water.
- We have produced small microparticles with large pores throughout, which are analogous in structure to honeycombs or whiffle balls. Using these microparticles, we are developing our PDDS technology, which may enable the delivery of drugs via the pulmonary route.

Our Strategy

In the last thirty years, a large worldwide market has emerged based on technologies that improve the delivery of established drugs in novel, cost-effective ways by providing significant benefits, such as improved safety and efficacy, increased patient compliance, greater ease of use, expanded indications or reduced cost. Drug delivery technologies can improve the commercial prospects for existing drugs by introducing new formulations that offer new delivery methods that may be patented and thereby protected. Traditionally, drug delivery companies have earned royalties by applying their delivery technologies to create new formulations of existing drugs owned by others. Recently, some companies have begun developing new drugs by using their proprietary drug delivery technologies in combination with off-patent drugs. These companies are often referred to as specialty pharmaceutical companies.

Our goal is to become a leading specialty pharmaceutical company that develops and commercializes new drugs and improved formulations of existing drugs using our porous microparticle technology. Our strategy to accomplish that goal includes the following:

Advance Development of Our Lead Product Candidate, AI-700. We are currently enrolling patients in a Phase III clinical trial program for our lead product candidate, AI-700, a cardiovascular drug for the detection of coronary artery disease. We intend to complete enrollment in these Phase III trials for AI-700 by the end of 2005 and submit a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, in the first half of 2006.

Focus on Proprietary Product Opportunities. We intend to focus on proprietary product opportunities, where we own broad patent rights to the products. Due to our ownership interest in these product candidates and technology, we believe we would be able to negotiate corporate collaborations from a stronger position than service-oriented companies that develop drug delivery technologies for patented drugs owned by pharmaceutical or biotechnology companies. We may retain the sales and marketing rights to our proprietary products in specialty markets that we can readily address. For instance, our lead product candidate, AI-700, will initially be used by a subset of cardiologists, called echocardiologists, who are generally hospital-based. We believe echocardiologists can be reached by a relatively small sales force of approximately 60 to 100 people in the United States. Therefore, we believe AI-700 may be an attractive candidate for us to market and sell directly in the United States. We intend to pursue strategic partnering opportunities to market and sell AI-700 outside of the United States.

Apply Our Proprietary Technology as Delivery Systems for Patented Drugs. We believe that our porous microparticle technology can be applied to a wide variety of FDA-approved and development stage drugs, as well as patented and off-patent drugs. Many patented drugs owned by large pharmaceutical companies are hydrophobic or delivered by inhalation. These drugs could benefit from our HDDS and PDDS technologies. We plan to seek collaborations with companies that have patented drugs that could benefit from the most compelling capabilities of our technologies. By focusing on drugs where the advantages of our technologies are most compelling, we believe we will be in an attractive position when negotiating the terms of these collaborations.

Focus on Large Markets Where Our Product Candidates Can Address Significant Unmet Clinical Needs. We are focused on developing proprietary drugs for large markets within cardiology, oncology and asthma where we believe our porous microparticle technology can provide compelling clinical advantages over current approaches. For example, we believe our lead product candidate, AI-700, will provide a low cost and convenient alternative for the detection of coronary artery disease. We believe the potential market opportunity for AI-700 is approximately $1.9 billion.

Product Development Programs

We are employing the capabilities of our proprietary porous microparticle technology to develop product candidates that address large unmet clinical needs within cardiology, oncology and asthma.

AI-700, Intravenous Delivery of Gas for Ultrasound Contrast

Broad Applications for Ultrasound Contrast. We have developed an intravenous delivery system for gas that has the potential to expand the usefulness of ultrasound in the detection of coronary artery disease. Ultrasound is one of the least expensive and most frequently used imaging techniques that permit physicians to view the inside of the body. However, ultrasound is the only frequently used imaging technique without a commercially significant contrast agent. As a result, the clarity of ultrasound is often inadequate for a definitive assessment of medical conditions. A contrast agent that could provide more detail and clarity and thereby improve the diagnostic image produced could expand the usefulness of ultrasound. Gases are attractive contrast agents for ultrasound because they reflect ultrasound waves more efficiently than blood or body tissues, enabling their detection by the ultrasound machine. Gas injected intravenously can potentially act as a tracer of abnormal blood flow, which is associated with many life-threatening diseases such as coronary artery disease. However, gas rapidly dissolves in blood thereby losing its effectiveness. As a result, microparticles that can entrap the gas and be administered intravenously are necessary in order to develop an ultrasound contrast agent with broad applications.

Coronary Artery Disease Market. According to the American Heart Association, or AHA, almost 13.0 million people in the United States suffer from coronary artery disease, the leading cause of death in the United States. Coronary artery disease is characterized by the accumulation of plaque, which narrows coronary arteries and reduces blood flow in the heart muscle. The AHA projects that in 2003, approximately $61.0 billion was to be spent on direct medical expenses for coronary artery disease in the United States. Early detection of coronary artery disease can reduce treatment costs, increase patient survival and improve quality of life.

The definitive method for the detection of coronary artery disease is coronary angiography, an expensive and invasive procedure impractical for use as a routine screening tool. Two of the most common methods for coronary artery disease screening are nuclear stress imaging and stress echocardiography, which is ultrasound of the heart. We estimate that 9.5 million of these screening procedures were performed collectively in the United States in 2002. We believe that a contrast agent that enables the assessment of blood flow in the heart muscle, or myocardial perfusion, with ultrasound could replace each of these screening procedures. We believe that an ultrasound contrast agent capable of myocardial perfusion assessment could be priced at $100 per vial. In myocardial perfusion assessment we anticipate two vials will be used per procedure, one at stress and one at rest. Assuming all of these procedures were performed using ultrasound with an effective contrast agent at a price of $200 per procedure, we estimate the potential U.S. ultrasound contrast market for the cardiac indication of A1-700 to be approximately $1.9 billion.

Current Practice for Coronary Artery Disease Screening. Nuclear stress tests assess myocardial perfusion, or blood flow in the heart muscle. Nuclear stress tests involve the intravenous injection of a radioactive compound, followed by scans of the heart using a special camera while the patient is at rest and under stressed conditions. These tests typically take about five hours to complete, cost approximately $935 per procedure, and due to significant capital equipment costs and complex regulatory requirements

associated with the use of radioactive materials, are not available in many hospital or physician office settings. We estimate that 7.0 million nuclear stress tests were conducted in the United States in 2002.

Stress echocardiography, or stress echo, assesses the motion of the heart wall. Advanced coronary artery disease typically results in abnormal blood flow in the heart muscle, which in turn causes abnormal wall motion that can be detected by the ultrasound machine used in stress echo. Although myocardial perfusion information from nuclear stress tests provides the most direct information about blood flow in the heart muscle, stress echo provides dynamic, real-time information about regional heart function. This additional information, along with the greater availability of ultrasound over nuclear equipment, results in the use of stress echo as a screening method in many hospital and physician office settings. Stress echo involves the use of high-frequency sound waves that are bounced off of the heart wall while the patient is at rest and under stressed conditions. We estimate that 2.5 million stress echo procedures were conducted in the United States in 2002. However, stress echo is often inadequate for a definitive assessment of coronary artery disease. For instance, the motion of the heart wall can be difficult to see under stress conditions, particularly in obese patients. In addition, stress echo without use of a contrast agent cannot detect myocardial perfusion.

There is no ultrasound contrast agent approved by the FDA for use in stress echo or myocardial perfusion imaging. Ultrasound contrast agents have been approved by the FDA for left ventricular opacification, referred to as a resting wall motion study, which is a procedure for looking at the heart wall and chambers while the patient is at rest. However, we believe that this indication has limited clinical utility because ultrasound is usually capable of assessing resting wall motion without a contrast agent. We estimate that less than 20% of all resting echocardiograms require a contrast agent for resting wall motion assessment.

Our Solution, AI-700, a Synthetic Polymer Microparticle. Using our porous microparticle technology, we specifically designed AI-700 for myocardial perfusion assessment. Currently in Phase III clinical trials, AI-700 is an ultrasound contrast agent that is being developed to enable stress echo to provide information on myocardial perfusion in addition to wall motion. Based on the results of our Phase II clinical trials, we believe that stress echo with AI-700 has the potential to provide information comparable to the nuclear stress tests, while retaining the advantages of ultrasound.

We believe we have overcome many of the limitations of other ultrasound contrast agents by developing an intravenous gas delivery system made from a synthetic polymer. All of the ultrasound contrast agents currently approved by the FDA for resting wall motion assessment deliver gas intravenously in fragile systems made from natural materials. When exposed to the power of the ultrasound beam during the imaging procedure, these natural materials are so fragile they rupture and release the gas into the blood where it dissolves, thereafter rendering these contrast agents ineffective. Moreover, some ultrasound contrast agents encapsulate nitrogen, which dissolves quickly in water. Such contrast agents have a very short duration of enhancement because the nitrogen is quickly pushed out of the microbubble and displaced with water. Ultrasound contrast agents made from natural materials or containing nitrogen have only been approved by the FDA for resting wall motion assessment and we believe they are difficult to use in myocardial perfusion imaging, which is more technically demanding.

Unlike the natural materials used in FDA-approved ultrasound contrast agents, the synthetic polymers used in AI-700 do not break during the imaging procedure. In addition, perfluorocarbon gases are less soluble in water and therefore have the propensity to stay inside the microparticle. As a result, we can deliver a higher concentration of gas to the myocardium over a longer period of time, thereby enabling AI-700 to target the broader application of myocardial perfusion assessment. AI-700 is a dry powder consisting of small, hollow microparticles filled with a perfluorocarbon gas. These microparticles have low porosity outer shells made of a synthetic biodegradable polymer, called poly (D, L-lactide co-glycolide), or PLGA, that has been used in other drug delivery systems approved by the FDA. The composition and structure of the outer shell, which contains a phospholipid, and the properties of the perfluorocarbon gases slow the rate at which the gas dissolves and prevent the microparticles from being quickly broken down inside the body. These microparticles are suspended in sterile water and injected into the body by a single

intravenous injection prior to ultrasound imaging. AI-700 was designed to be easy to use with commercially available ultrasound equipment and established imaging techniques.

Potential Benefits of Stress Echo with AI-700 vs. Nuclear Stress Tests

Stress echo with AI-700 has the potential to significantly reduce the time, cost and resources needed in the assessment of myocardial perfusion.

- *Less Expensive.* We estimate that the cost of performing an ultrasound imaging procedure using our AI-700 contrast agent will be approximately $400 per procedure, representing costs of $200 for the contrast agent and $200 for administering the procedure. Nuclear stress tests typically cost approximately $935 per procedure. Nuclear stress tests are relatively more expensive because the equipment is large and costly and patient throughput is low. Ultrasound equipment is much smaller and generally half the cost of nuclear equipment used for the detection of coronary artery disease.
- *Less Time Consuming.* Nuclear stress tests typically take five hours, while ultrasound procedures typically take 30 minutes.
- *Greater Availability.* Due to the technical complexity, high cost and the regulatory requirements associated with the use of radioactive materials, nuclear stress tests are not available in all hospitals, cardiology practices and emergency departments. In the United States, ultrasound equipment is widely available in all of these settings.
- *More Information.* Stress echo with AI-700 has the potential to provide information on both myocardial perfusion and wall motion, whereas nuclear stress tests typically provide information only on myocardial perfusion.
- *No Radioactivity.* AI-700 is made from a synthetic polymer that does not require special licensing, has at least a two-year shelf life, and is convenient to use and store. Nuclear stress tests use radioactive materials that create additional costs due to preparation, storage and disposal requirements.
- *Expanded Opportunity for Cardiologists.* We believe that many cardiologists will prefer ultrasound with AI-700 over nuclear stress tests because it may allow them to remain in closer contact with their patients. To assess myocardial perfusion with nuclear stress tests, many patients are referred by cardiologists to the radiology department, which is usually a different profit and care center within the hospital.

Potential Benefits of Stress Echo with AI-700 vs. Stress Echo without Contrast

Stress echo with AI-700 has the potential to provide broader information for cardiological evaluation.

- *More Information.* Stress echo with AI-700 has the potential to provide information on both myocardial perfusion and wall motion, whereas stress echo without contrast provides information only on wall motion.
- *Potential for Increased Sensitivity with Perfusion.* Cardiologists seek to identify coronary artery disease early in the disease progression in order to minimize the risk of heart attack. In early coronary artery disease, the coronary artery is only partially blocked, so there may be little or no wall motion abnormality, but there could be a perfusion abnormality. The potential for increased sensitivity has contributed to the popularity of nuclear stress tests. We estimate that in 2002, 7.0 million nuclear stress tests were performed versus 2.5 million stress echo tests without contrast. We believe that an ultrasound contrast agent capable of myocardial perfusion imaging would enable stress echo to compete more effectively with nuclear stress testing.

Clinical Results. We enrolled over 200 human subjects in our Phase I and Phase II clinical trials for AI-700. Our Phase I clinical trials evaluated the safety and feasibility of myocardial perfusion imaging with AI-700. Our Phase II clinical trials evaluated the preliminary safety and efficacy of AI-700 enhanced

ultrasound imaging. In our Phase II clinical trials, efficacy was measured by comparing the results obtained from myocardial perfusion assessment using AI-700 enhanced ultrasound with those obtained using nuclear stress tests. Our Phase I and Phase II clinical trials were conducted in the U.S. under an Investigational New Drug Application, or IND, with the FDA. The results of our Phase II trials are summarized below. We have filed these results and our protocol for our Phase III trials with the FDA. We initiated our Phase III program in early 2003. We initiated the pivotal phase of our Phase III program at selected sites in late 2003. We plan to cumulatively enroll 300 patients in the Phase III program by the end of 2004, to complete total patient enrollment in the Phase III program by the end of 2005, which enrollment we estimate to be approximately 600 patients in the pivotal phase of our Phase III program, and to file an NDA for AI-700 in the first half of 2006. Although these milestones and target completion dates reflect our current plans, we cannot assure you that we will complete these milestones on this schedule, or at all.

The "20" Trial. Our objectives in the "20" trial were to evaluate the safety of AI-700 in subjects with known coronary artery disease and to determine the optimal imaging procedures for myocardial perfusion assessment using AI-700 enhanced echocardiography. The study included 53 subjects, was conducted by echocardiologists and utilized a variety of commercially available equipment platforms. Subjects enrolled in the "20" trial received a single injection of AI-700 at a variety of doses and were imaged under resting conditions only. The primary efficacy endpoint was agreement between echocardiography with AI-700 and nuclear stress. Agreement was defined as the percentage of subjects who received the same diagnosis using AI-700 enhanced echocardiography as with nuclear stress tests. At the optimal imaging conditions identified during the trial, we met the primary endpoint of this trial.

The "21" Trial. Our objectives in the "21" trial were to evaluate the safety and diagnostic efficacy of AI-700 in patients with suspected or confirmed coronary artery disease as well as in healthy subjects. The study included 122 subjects, was conducted by echocardiologists and utilized a variety of commercially available ultrasound equipment platforms and imaging techniques. A variety of doses of AI-700 were evaluated in the trial. Patients enrolled in the "21" trial received two injections of AI-700, one under resting conditions and the other under stressed conditions. All patients received a nuclear stress test and either a stress echo with AI-700 or a stress echo without contrast. The primary efficacy analysis was based on the ability of independent echocardiologists, blinded to all other information, to detect myocardial defects when comparing stress echo images to nuclear stress. In the "21" trial we met the primary efficacy endpoints, which were sensitivity, or the ability to detect disease, and specificity, or the ability to determine the absence of disease.

Efficacy data. Comparison of stress echo with AI-700 and nuclear stress for subjects in our Phase II trials indicated the following:

- *Stress echo with AI-700 versus stress echo without contrast.* Stress echo with both low and high doses of AI-700 resulted in a 30% or greater increase in sensitivity compared to stress echo without contrast, and demonstrated a higher level of agreement with nuclear stress tests versus stress echo without contrast.

- *Stress echo with AI-700 versus the nuclear stress test.* Stress echo with both low and high doses of AI-700 agreed with nuclear stress tests in more than three-quarters of all patients.

- *Stress echo with AI-700 versus coronary angiography.* Nuclear imaging does not always result in a correct diagnosis of coronary artery disease. The generally agreed gold standard for the diagnosis of coronary artery disease is coronary angiography. In a retrospective exploratory analysis of those patients that underwent coronary angiography, stress echo with AI-700 had the same agreement as nuclear stress tests when compared to coronary angiography.

Safety Data. None of the subjects in our Phase I and II clinical trials have had serious adverse experiences after the administration of AI-700. The majority of the adverse experiences observed after administration of AI-700 have been mild in intensity and of short duration.

The Phase III Program: Detection of Coronary Disease in Patients Being Evaluated for Ischemic Heart Disease. Under a U.S. IND and in compliance with applicable European regulatory requirements, our Phase III program for AI-700 commenced in early 2003 and the pivotal phase of our Phase III program commenced at selected sites in late 2003. Before beginning the Phase III program, we had extensive discussions with the FDA, and have attempted to address its questions and incorporate its comments into our protocols and endpoints. The Phase III clinical plan provides for a two-part program consisting of a pilot phase, which is currently ongoing at multiple clinical sites and is designed to qualify and train new investigators, and two multi-center pivotal trials each of approximately 300 patients with suspected coronary artery disease. As of March 1, 2004, over twenty clinical sites, located in North America and Europe, had been initiated in the Phase III program. Clinical sites which demonstrate readiness in the pilot phase are advanced on a rolling-basis into the pivotal phase, such that certain clinical sites are currently participating in the pivotal phase while others are at varying stages of progress in the pilot phase. Safety will continue to be tested and evaluated during our Phase III program. Data from the trials are intended for submission to U.S., Canadian and European regulatory authorities. The endpoints for the trial are sensitivity and specificity in comparison to nuclear stress testing, angiography or clinical outcome. For the Phase III trials, the primary efficacy endpoints relative to nuclear stress tests and angiography are set at thresholds that are the same or lower than those already achieved in our Phase II trial results. Although we are targeting these clinical endpoints in our Phase III trials, we cannot assure you that we will successfully achieve results that meet or exceed these clinical endpoints.

Future Indications. Since AI-700 circulates in the blood and acts as a tracer of blood flow, we believe it has the potential to assist in the diagnosis of a wide variety of diseases in addition to coronary artery disease. Abnormal blood flow is associated with several life threatening diseases including various forms of cancer, renal artery stenosis and deep vein thrombosis. These diseases often cannot be adequately assessed with ultrasound imaging without contrast, and as a result radiologists currently detect these diseases with more expensive imaging techniques, such as computerized tomography, angiography, nuclear medicine and venography. Ultrasound imaging using AI-700 may offer a cost-effective alternative to these expensive techniques.

Products from Our Hydrophobic Drug Delivery System, or HDDS

Broad Applications for the Delivery of Hydrophobic Drugs. We have developed a proprietary formulation technology called HDDS that converts drugs that do not dissolve well in water, or hydrophobic drugs, into microparticles or nanoparticles of the drugs embedded in small microparticles such that the drugs can rapidly dissolve in water. Formulation of hydrophobic drugs is often challenging. Since the human body is primarily composed of water, hydrophobic drugs do not dissolve well in the body, which can limit the effectiveness of these drugs. Many promising drugs never make it to market because they are difficult to dissolve. Drug programs are often abandoned after significant investment because suitable formulations for these insoluble drugs are elusive. Many hydrophobic drugs that do make it to market have less than ideal formulations. Developing intravenous formulations of hydrophobic drugs is particularly challenging. Possessing intravenous formulations of drugs can open new markets for drugs like antibiotics that could often be initially prescribed in a hospital setting. In addition, intravenous formulations can expand the market for the oral dosage formulation because physicians typically prefer to discharge patients on the oral formulation of the intravenous formulation administered to the patient in the hospital.

Market for Hydrophobic Drug Delivery. We believe that FDA-approved hydrophobic pharmaceuticals generated $108 billion in revenues in 2000 and constituted up to 40% of all drugs in development. Taxol, a leading cancer drug with worldwide revenues of $934 million in 2003, is an example of a hydrophobic drug with a less than ideal formulation.

Current Practice. Many hydrophobic drugs are comprised of particles that are relatively large and therefore have a limited surface area available for interaction with water. These hydrophobic drugs are often formulated in less than ideal ways in order to make them dissolve. It is possible to increase the dissolution rate of hydrophobic drugs by increasing their aggregate surface area. To accomplish this, many

pharmaceutical companies use a process, called micronization, which entails grinding hydrophobic drugs into smaller microparticles. However, the drug particles produced by micronization are often still not small enough to adequately improve dissolution, or to be administered intravenously. Alternatively, oils like Cremophor are used to dissolve the drugs. However, these oils are often not well tolerated and can require prolonged infusion rather than rapid injections. In addition, some hydrophobic drugs can be formulated into soft gelatin capsules, but these are only suitable for oral administration and encapsulate only a small volume of drug, requiring the administration of many capsules. Sometimes development of these drugs must be terminated because no suitable formulation can be found.

Our Solution: Rapidly Dissolving Sponge-Like Particles. We have demonstrated that our HDDS technology improves the dissolution rate of a variety of hydrophobic drugs. HDDS has achieved up to 30-fold increases in the dissolution rate of a variety of hydrophobic drugs. HDDS has produced drug formulations that are well-tolerated in pre-clinical studies and we believe would be suitable for all routes of administration, without resorting to the use of unsafe or unproven additives to formulate the drug.

AI-850, Our Improved Formulation of Paclitaxel. AI-850, our initial product candidate utilizing our HDDS technology, is a readily dissolving formulation of the hydrophobic drug, paclitaxel, the active ingredient in the cancer drug, Taxol. To dissolve paclitaxel, Taxol contains Cremophor, which is believed to cause severe hypersensitivity reactions, such as an extreme allergic reaction called anaphylaxis. Therefore, Taxol is typically administered using pre-medications and by long infusions to patients with cancer. By putting paclitaxel into our sponge-like microparticles, we have created a paclitaxel formulation that is free of Cremophor. In our Phase I clinical trial of AI-850, patient pre-medication is not required as part of the study protocol.

Potential Benefits of AI-850 Over Taxol. We believe that our pre-clinical studies demonstrate significant potential benefits of AI-850 over Taxol and its generic, Cremophor-based competitors. These potential benefits include increased tolerance, shorter administration and increased efficacy at higher dose.

Product Development Status. Under a U.S. IND, we commenced a Phase I clinical trial in 2002 of AI-850. This is a dose escalation study designed to determine the maximum tolerated dose of AI-850. Doses currently being evaluated in patients in the Phase I study are higher than the doses of paclitaxel customarily delivered using the same dosing schedule for the treatment of metastatic breast cancer. We expect to complete this study in 2004.

Future Hydrophobic Drug Delivery Product Candidates. In 2003, in conjunction with a large pharmaceutical company, we initiated a feasibility study for the potential application of our HDDS technology in order to create an intravenous formulation of a patented drug approved by the FDA for oral administration. An intravenous formulation of this drug may enable the drug to address a new indication for a life-threatening disease that is treated in the hospital setting. If the feasibility study is successful, we anticipate that we will enter into a research and development agreement with this pharmaceutical company. We have demonstrated that our HDDS technology improves the dissolution rate of a variety of orally administered, intravenously administered and inhaled hydrophobic drugs, including COX-2 inhibitors, taxanes, calcium channel blockers and anti-fungals. We will seek opportunities to work with other companies on improving their patented hydrophobic drugs and product candidates. In addition, we will evaluate the feasibility of developing, on our own or in collaboration with others, improved formulations of off-patent hydrophobic drugs.

Products from Our Pulmonary Drug Delivery System, or PDDS

Broad Applications for Sustained Release in the Lung. We are developing a sustained release delivery system for drugs delivered locally to the lung, which is desirable for the treatment of respiratory disease. Relative to systemic drug delivery via the oral or injectable route, local delivery of respiratory drugs via the pulmonary route requires smaller doses of the drug and minimizes systemic toxicity because it can be delivered directly to the site of the disease. Moreover, sustained release of respiratory drugs may offer significant clinical benefit to millions of respiratory patients, including a growing percentage of pediatric patients. Sustained release drugs may allow patients to take treatments for such diseases as

asthma less frequently, and to receive more prolonged and steadier relief. We believe sustained delivery of drugs to the lung also offers the potential for improved safety, by moderating the drug peaks and troughs of immediate release drugs, which can cause added toxicity or reduced efficacy. Our initial development efforts have focused on developing sustained release formulations of asthma drugs.

Respiratory Market. The worldwide 2002 market for inhaled respiratory drugs was $8.0 billion. We believe the delivery of long-acting drugs to the lungs represents a significant medical opportunity. We are not aware of any other sustained release respiratory drug that has been approved or is in clinical trials. We are developing AI-128, an improved formulation of an approved asthma drug that is off-patent. The approved asthma drug generated revenues in excess of $500 million in 2003.

Current Practice. Current pulmonary delivery systems are not ideal, delivering inaccurate doses, requiring frequent dosing and losing significant amounts of drug in the delivery process. Most asthma drugs delivered via inhalation are immediate release formulations that must be inhaled multiple times per day, which discourages patient compliance. When patients forget to take their medicine during the day, they may experience complications which may result in increased emergency room visits and hospitalizations. In a recent study, two thirds of all asthma patients did not take their medications as directed. In addition, immediate release formulations often deliver drug levels that peak and trough, causing undesirable toxicity or inadequate efficacy.

Our Solution: Slowly Dissolving Whiffle Ball-Like Microparticles. By controlling particle size, particle porosity and thus density, and particle composition, and therefore the aerodynamic properties of a particle, our PDDS technology controls where drug particles go in the lung and how quickly they release their drug. This tight control of release rate, and targeting within the lungs, may enable our PDDS technology to address many of the hurdles of sustained release pulmonary delivery.

AI-128, Our Improved Formulation of an Asthma Drug. AI-128 is our initial product candidate utilizing our PDDS technology. AI-128 is a sustained release, dry powder formulation of a widely used asthma drug. We believe that AI-128 is the first human demonstration of sustained release drug administration in the lung. AI-128 was originally developed as part of a joint venture with Elan Corporation, plc and affiliates established in 2000. In 2002, for reasons beyond our control, and, to our knowledge, not based on Elan's perception of the performance or prospects of our technology, Elan ceased funding the joint venture, and the joint venture was terminated. In connection with the termination, we agreed to pay Elan a royalty if we commercialize AI-128.

Potential Benefits over Approved Formulations. With once-a-day dosing, we believe the product would be more convenient for the patient, reducing non-compliance related complications and costs. By controlling the release rate of the drug to the lung, AI-128 offers the potential for improved safety. Slowing drug release in the lung offers the potential for a lower peak concentration of drug in the systemic circulation.

Clinical Results. We completed a European Phase I clinical trial with AI-128. The study was conducted in accordance with applicable local regulatory requirements. In this trial, we demonstrated that approximately 80% of inhaled AI-128 was delivered to the intended target, the upper lung. These trials also demonstrated that the microparticles remained in the lung for up to 24 hours, the period of time that we believe is required for once-daily dosing, and that the drug was released from the microparticles in the lung over a 12 to 24-hour period.

Future Applications. We believe our PDDS technology may enable improved formulations of other asthma drugs as well as allow drugs that must be delivered into the bloodstream for systemic delivery to be administered by inhalation through the lung. We have demonstrated in pre-clinical studies that we can create sustained release, dry-powder reformulations of drugs currently used to treat respiratory disease. We believe that one or more of such reformulations could have many of the benefits AI-128 potentially offers. Moreover, many large molecule drugs, such as proteins, cannot be delivered orally because they are destroyed by enzymes in the gastrointestinal system. As a result, they often must be injected subcutaneously or intramuscularly several times per week in order to get an adequate amount of the drug

into the body's general circulation. Since the lung does not contain these destructive enzymes, delivery of these drugs via the pulmonary route could be more convenient and require less dosing. We plan to seek both proprietary and collaborative opportunities for these drug formulations.

Our Proprietary Microparticle Technology

Microparticles are useful in the delivery of a wide range of drugs. Suitability of microparticles for use in pharmaceuticals depends on a variety of factors, including size and porosity. Smaller microparticles have a broader range of utility, such as intravenous and pulmonary delivery applications. Depending on the targeted site and desired route of delivery, drug delivery technologies utilize microparticles of various sizes. Our porous microparticle technology enables us to produce very small microparticles that are smaller than a red blood cell and with a wide range of porosities.

Microparticle Size

Large microparticles are microparticles over 100 microns in size. Large microparticles are used to deliver drugs through relatively large orifices, like the mouth (oral delivery). Large microparticles have been used in the delivery of both immediate and controlled release oral drug formulations. However, these particles cannot be delivered by injection, because they are too large to fit through a needle. In addition, they are unsuitable for delivery via the pulmonary route, because larger particles tend to get caught in the back of the throat when inhaled. For these reasons, the use of large microparticles is generally limited to oral administration.

Medium microparticles are microparticles between 10 and 100 microns in size. These particles are small enough to fit through a needle, and therefore are suitable for injection subcutaneously, which is under the skin, or intramuscularly, which is into the muscle. These microparticles have been used primarily to deliver drugs, which cannot be delivered orally because they are destroyed in the gastrointestinal system. However, medium microparticles cannot be injected intravenously because they are too large to fit through the body's smallest blood vessels, or capillaries, and like large microparticles, are unsuitable for delivery via the pulmonary route.

Small microparticles are microparticles smaller than 10 microns, which is approximately the size of a human red blood cell. Small microparticles include nanoparticles, which are particles smaller than 1 micron. Small microparticles are small enough to pass through the capillaries for intravenous delivery; are small enough to be readily inhaled for pulmonary delivery; and have more total surface area per unit of weight relative to larger microparticles, making them a particularly efficient method for delivering hydrophobic drugs. Intravenous delivery is desirable in a hospital setting to ensure that the drug is fully bioavailable, or that the entire drug dose is absorbed by the body. Intravenous delivery is also used for drugs that must be injected but with a dose too high for intramuscular or subcutaneous delivery. Drugs are also administered intravenously, or directly into the blood, to act as tracers of blood flow, since abnormal blood flow is associated with many life threatening diseases. Therefore, small particles have many potential applications, including use as ultrasound contrast agents, as delivery systems for hydrophobic drugs, and as delivery vehicles for asthma drugs.

Microparticle Porosity

The ability to vary the porosity of microparticles on a consistent basis can be critical to the successful use of microparticles in pharmaceutical products. For instance, in ultrasound contrast imaging, we believe it is advantageous to use microparticles that are highly porous on the inside but with limited porosity in the shell. Porosity on the inside of microparticles enables them to deliver more of the active ingredient, which is gas, than particles that are dense. Limiting porosity in the shell prevents gas leakage and enables the retention of the gas inside the particle. Furthermore, pores can facilitate absorption of water into a microparticle, which is useful in getting hydrophobic drugs to dissolve more quickly, and useful for controlling the release of a drug from a sustained release system. Finally, in drug delivery to the lung, it is

advantageous to use microparticles of various porosities, which controls density, because the size and density of the microparticles dictates where in the lung they will be delivered.

Microparticle Production Using Spray Drying

We believe the use of small, porous microparticles has not reached its full potential in the delivery of drugs. We believe that processes for creating small microparticles have low yields, have not been adapted for use with encapsulating materials like synthetic polymers, have low encapsulation efficiency and are difficult to combine with other technologies, such as coating technologies. We believe that the use of porosity to improve drug formulations has been underutilized because an efficient process for creating porous microparticles at commercial scale did not exist. Our porous microparticle technology was designed to address the limitations of existing processes.

Spray drying is a production technique widely used in the pharmaceutical industry because it is a single-step, continuous process. However, standard spray drying:

- *Produces solid microparticles* rather than the porous microparticles, which are required for ultrasound contrast imaging and may be beneficial for hydrophobic and pulmonary drug delivery.
- *Does not completely remove* moisture from the microparticles, contributing to low yields and making standard spray drying uneconomic for the production of drugs made from expensive raw materials.
- *Results in high levels of residual solvents*, which can be problematic for the stability and safety of the drug.
- *Often operates at high temperatures*, making it difficult to use with drugs that are unstable at higher temperatures.
- *Is not well-suited to sterile, or aseptic, processing*, which is required for most intravenously administered drugs and is beneficial for pulmonary-delivered drugs.

Our proprietary porous microparticle technology platform consists of two key components — a multi-chamber spray dryer and pore forming agents.

Our Patented Spray Dryers

We believe we have overcome the limitations of standard spray drying in producing small microparticles and nanoparticles through patented equipment innovations that:

- *Remove nearly all residual solvents such as moisture* from the microparticles because our patented spray dryer increases the length of time the microparticles are dried.
- *Can be operated at low or high temperatures*, due to increasing the drying time used for microparticles produced at lower temperatures, and reducing the drying time for microparticles produced at higher temperatures.
- *Are well suited to aseptic processing* by using steam sterilization techniques and a positive pressure system, thereby minimizing the contaminants pulled into the spray dryer from the surrounding environment.

We have improved the drying capability of standard spray dryers by adding additional drying chambers through which the microparticles travel. The additional drying chamber contains a large, narrow coil through which the particles can be dried at multiple temperatures and at high linear gas velocities. As a result our spray dryers allow high throughput drying, higher yield and lower solvent than conventional spray dryers do. The additional drying chamber allows the microparticles to remain in the drying phase for a longer period of time, thereby increasing the amount of moisture and residual solvents that are removed during the drying phase. This innovation, which is the subject of three of our issued patents, improves yield by reducing the amount of microparticles that cling to the surfaces of the spray dryer due to

inefficient drying. Accordingly, we believe that this technology is appropriate for the encapsulation of drugs using expensive raw materials. This innovation enables us to increase the drying time and lower the drying temperature for drugs. Accordingly, we believe this technology is appropriate for the encapsulation of drugs, like proteins, which are unstable at higher temperatures.

In order to produce microparticles and nanoparticles to be used in drugs delivered intravenously, the particles must be produced aseptically. We have improved standard spray dryers by making them suitable for aseptic processing. Our spray dryers operate under positive pressure, minimizing the risk of pulling contaminants into the process from the surrounding environment. In addition, our spray dryers are composed of stainless steel and Teflon components to mitigate against shedding into the product during processing, and can be sterilized using steam sterilization techniques.

We have made these improvements to standard spray drying processes and equipment without altering the fundamental advantages of standard spray drying. Like standard spray dryers, our spray dryers enable a single-step, continuous process that is efficient in encapsulating up to 100% of the active ingredient, and can be used with either synthetic or natural materials.

Our Patented Pore Forming Agents

We have developed a patented process technology for creating porous microparticles. To create pores in our microparticles we add pore forming agents to the solution before we put it through the spray dryer. These pore forming agents create bubbles, similar to the bubbles in carbonated beverages. These bubbles are formed while the solution is being converted into a microparticle in the spray dryer. The bubbles create pores in the microparticle and the pore forming agents are removed during the drying process. We can vary the number and size of the pores by varying the amount of pore forming agents we add to the process. In this way we can design microparticles that are hollow or sponge-like.

Reimbursement

We intend to focus on obtaining coverage and reimbursement from Medicare, Medicaid and private insurers for our product candidates. Although there can be no assurance that we will be successful in obtaining third-party reimbursement, we believe we will be successful in obtaining this reimbursement for our lead product candidate, AI-700.

Effective January 2001, the Centers for Medicare and Medicaid Services, formerly known as the Health Care Financing Administration, implemented a reimbursement code that provides for reimbursement for the use of injectable contrast material in echocardiography in a physician's office and hospital outpatient setting. The current reimbursement rate for ultrasound contrast agents used in echocardiography varies slightly by state but is generally 95% of the average wholesale price. As of May 2003, the reimbursed rate for the FDA-approved ultrasound contrast agents for resting wall motion assessment was over $100 per vial. Although private insurers make their own decisions on reimbursement, they typically follow the lead of the Centers for Medicare and Medicaid Services, which manage reimbursement for Medicare and Medicaid.

We plan to apply for a new reimbursement code at a higher rate. We believe ultrasound imaging using AI-700 for myocardial perfusion assessment, which we anticipate will require two vials per study, will provide at least the same clinical information as nuclear stress tests, but at much lower total study cost. Given these expected cost advantages, we believe that AI-700 will ultimately obtain adequate reimbursement in this era of managed care, where the federal government and private insurers are striving to lower the total cost of delivering state-of-the-art healthcare. Further, in the treatment of hospital inpatients, who are usually subject to a fixed total reimbursement based solely on their diagnosis and not on the test used, we expect that hospital staffs will be encouraged to use the much lower cost ultrasound test with AI-700, if and when it is approved by FDA, rather than the expensive nuclear test. Our efforts to obtain a higher reimbursement rate can begin prior to our product's approval and will probably require about two years for completion. The current reimbursement codes cover hospital outpatient and physician offices, which are the locations where almost all stress echoes are performed. In the period immediately

following the potential launch of our product, we believe that the current reimbursement rates for ultrasound contrast agents would enable us to sell our product at attractive margins.

Manufacturing

We currently outsource the production of our products used in our clinical trials to qualified third parties. For example, we have contracted with Hollister-Stier Laboratories for the production of the clinical trial materials to be used in our Phase III clinical trials for AI-700 and our Phase I clinical trials for AI-850. These third-party manufacturing facilities must comply with current good manufacturing practices, or cGMPs, enforced by the FDA. In preparation for commercial readiness, we are currently evaluating the extent to which we want to continue to build our manufacturing capability through qualified third parties versus the potential cost and control advantages of relocating all or a portion of this manufacturing to an environment created and directly managed by us. We currently plan to manufacture products for our clinical trials at FDA-approved cGMP compliant facilities in the United States. We have identified potential primary and secondary suppliers of the raw materials used in the production of AI-700 and are in the process of scaling the manufacturing process in preparation for commercial production. We plan to manufacture some future materials, in particular for pre-clinical toxicology testing, at our production facilities in Watertown, Massachusetts.

Patents and Proprietary Rights

Our success depends in part on our ability to obtain patents, to protect trade secrets, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business.

As of March 1, 2004 , we own fourteen issued U.S. patents, one allowed U.S. patent application and eleven U.S. patent applications. Five of our issued U.S. patents are directed to aspects of our AI-700 product candidate. Three of our issued U.S. patents are directed to aspects of the spray drying method for manufacturing microparticles. Two issued U.S. patents, one allowed U.S. patent application and seven U.S. patent applications are related to various aspects of our porous microparticle drug delivery technology. Four issued U.S. patents and four U.S. patent applications relate to the AI-850 product and the delivery of other hydrophobic drugs. We also own a number of pending international and foreign patent applications corresponding to these U.S. patents and applications. As of the date of this Annual Report, our issued U.S. patents are listed below:

U.S. Patent No.	Date Issued	Expiration Date	Subject
5,611,344	March 18, 1997	March 5, 2016	Microencapsulated fluorinated gases for use as imaging agents.
5,837,221	November 17, 1998	July 29, 2016	Polymer-lipid microencapsulated gases for use as imaging agents.
5,853,698	December 29, 1998	March 5, 2016	Method for making porous microparticles by spray drying.
6,045,777	April 4, 2000	June 30, 2017	Method for enhancing the echogenicity and decreasing the attenuation of microencapsulated gases.
6,132,699	October 17, 2000	March 5, 2016	Microencapsulated fluorinated gases for use as imaging agents.
6,223,455	May 1, 2001	May 3, 2019	Spray drying apparatus and methods of use.
6,308,434	October 30, 2001	May 3, 2019	Spray dry method.

U.S. Patent No.	Date Issued	Expiration Date	Subject
6,395,300	May 28, 2002	November 4, 2019	Porous drug matrices and method of manufacture.
6,423,345	July 23, 2002	February 22, 2019	Lipid polymer compositions for enhanced drug delivery.
6,560,897	May 13, 2003	June 15, 2019	Spray drying apparatus and methods of use.
6,589,557	July 8, 2003	November 4, 2019	Porous celecoxib matrices and methods of manufacture
6,610,317	August 26, 2003	May 25, 2020	Porous paclitaxel matrices and methods of manufacture thereof
6,645,528	November 11, 2003	November 4, 2019	Porous drug matrices and methods of manufacture thereof
6,689,390	February 10, 2004	February 22, 2019	Matrices Formed of Polymer and Hydrophobic Compounds for Use in Drug Delivery

Four of the above patents, 6,560,897, 6,589,557, 6,610,317 and 6,645,528 were issued during 2003 and one of these patents, 6,689,390, was issued in early 2004.

Our planned and potential products will be protected from unauthorized use by third parties only to the extent that they are covered by valid and enforceable patents or are effectively maintained as trade secrets. Patents owned by or licensed to us may not afford protection against competition, and our pending patent applications now or hereafter filed by or licensed to us may not result in patents being issued. In addition, the laws of some foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States.

The patent positions of companies like ours involve complex legal and factual questions and, therefore, their enforceability cannot be predicted with certainty. Our patent applications may not issue as patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization. Patent expiration could adversely affect our ability to protect future product development and, consequently, our operating results and financial position.

Because patent applications in the United States and many foreign jurisdictions are typically held in secret and not published until eighteen months after filing, we cannot be certain that we were the first to file for protection of the inventions set forth in these patent applications. Because publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in each of our issued or pending patent applications.

Our planned or potential products may be covered by third-party patents or other intellectual property rights, in which case we would need to obtain a license or sublicense to these rights to continue developing or marketing these products. Although from time to time we receive correspondence from and have discussions with third-parties concerning the patent position of such third-parties, as of the date of this Annual Report we have never received correspondence from any third-party regarding an allegation of infringement. Any required licenses or sublicenses may not be available to us on acceptable terms, if at all. If we do not obtain any required licenses or sublicense, we could encounter delays in product introductions while we attempt to design around these patents, or could find that the development, manufacture or sale of products requiring these licenses is foreclosed.

We know of U.S. and foreign patents issued to third parties that relate to aspects of our product candidates. We are aware of U.S. and foreign patents owned by third parties, including potential competitors, that arguably cover aspects of our AI-700 contrast agent, although based on advice from our patent counsel we believe that these claims are not infringed and/or are invalid. The owners or licensees of these patents may file one or more infringement actions against us. Any infringement action by the owners or licensees of these patents could cause us to incur substantial costs defending the lawsuits and could distract our management from our business, even if the allegations of infringement are unwarranted. A U.S. or foreign court may find that the relevant claims of the U.S. and foreign patents are valid and enforceable, and that the manufacture, use, sale, offer for sale or importation of the AI-700 product infringes these claims. If our AI-700 contrast agent is found to infringe a third party's patent, the patent owners or licensees could secure judgments that require us to pay substantial damages and/or injunctions or other court orders that could prevent us from making, using, selling, offering for sale or importing AI-700. They could also secure judgements that prevent our customers from using AI-700. We also know of patent applications and issued patents filed by other parties in the United States and various foreign jurisdictions that relate to some aspects of our other product candidates. These patents and patent applications, if issued, could subject us to infringement actions or require that we obtain licenses which may not be available under reasonable terms or at all, although based on advice from our patent counsel we believe that these claims are not infringed and/or are invalid.

Litigation may be necessary to defend against or assert claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us, or to determine the scope and validity of the proprietary rights of others. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Litigation or interference proceedings could result in substantial costs to and diversion of effort by us, and could have a material adverse effect on our business, financial condition and results of operations. These efforts by us may not be successful.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees and contractors. There can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Government Regulation

U.S. Regulatory Approval

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries regulate and impose substantial requirements upon the research, development, pre-clinical and clinical testing, manufacture, distribution, record keeping, reporting, storage, approval, advertising, promotion, sale and export of pharmaceutical products. We believe that our products will be regulated as drugs by the FDA.

The process required by the FDA under the new drug provisions of the Federal Food, Drug and Cosmetics Act before our products may be marketed in the United States generally involves the following:

- pre-clinical laboratory and animal tests performed under the FDA's Good Laboratory Practices regulation;
- development of manufacturing processes which conform to FDA-mandated cGMPs;
- submission and acceptance of an Investigational New Drug application, or IND, which must become effective before clinical trials may begin in the United States;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate in our intended use; and
- FDA review and approval of an NDA, prior to any commercial sale or shipment of a product.

The testing and approval process requires substantial time, effort, and financial resources and we cannot be certain that any approval will be granted on a timely basis, if at all.

Pre-clinical tests include laboratory evaluation of the product candidate, its chemistry, formulation and stability, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the pre-clinical tests, together with manufacturing information and analytical data, are then submitted to the FDA as part of an IND, which must become effective before we may begin human clinical trials. Pre-clinical tests and studies can take several years to complete, and there is no guarantee that an IND based on those tests and studies will become effective to permit clinical testing to begin. An IND becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the trials as outlined in the IND and imposes a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. Prior to initiation of clinical studies, an independent Institutional Review Board at each medical site proposing to conduct the clinical trials must review and approve each study protocol. Similar requirements exist in other countries where we may choose to perform clinical trials.

Human clinical trials are typically conducted in three sequential phases that may overlap:

- Phase I: The drug is initially introduced into healthy human subjects or patients and tested for safety and dosage tolerance. Absorption, metabolism, distribution and excretion studies are generally performed at this stage.
- Phase II: The drug is studied in exploratory therapeutic trials in a limited number of subjects with the disease or medical condition for which the new drug is intended to be used in order to identify possible adverse effects and safety risks, to determine the preliminary or potential efficacy of the product for specific targeted diseases or medical condition and to determine dosage tolerance and the optimal effective dose.
- Phase III: When Phase II evaluations demonstrate that a specific dosage range of the drug is likely to be effective and has an acceptable safety profile, confirmatory therapeutic Phase III trials are undertaken to demonstrate clinical efficacy and to further test for safety in an expanded patient population, often at geographically dispersed clinical study sites.

We cannot be certain that we will successfully complete Phase I, Phase II or Phase III testing of our product candidates within any specific time period, if at all. Furthermore, the FDA, the Institutional Review Board or the sponsor may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

A description of the manufacturing process and quality control methods, as well as results of pre-clinical studies, toxicology studies and clinical trials, among other things, are submitted to the FDA as part of an NDA for approval prior to the marketing and commercial shipment of the product. The FDA may deny a new drug application if all applicable regulatory criteria are not satisfied or may require additional data including clinical, toxicology or manufacturing data. Even after a new drug application is issued, the FDA may withdraw product approval if compliance with regulatory standards is not maintained or if safety problems occur after the product reaches the market. In addition, the FDA requires surveillance programs to monitor the consistency of manufacturing and the safety of approved products that have been commercialized. The agency has the power to require changes in labeling or to prevent further marketing of a product based on new data that may arise after commercialization. Similar requirements exist in other countries where we may choose to seek marketing approval.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially, based upon the type, complexity and novelty of the pharmaceutical product. Government regulation may delay or prevent

marketing of potential products altogether or for a considerable period of time and imposes costly and time-consuming requirements. We cannot be certain that the FDA or any other regulatory agency will grant approval for any of our products under development on a timely basis, if at all. Success in pre-clinical or early stage clinical trials does not assure success in later stage clinical trials. Data obtained from pre-clinical and clinical activities is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. Even if a product receives regulatory approval, the approval is typically limited to specific clinical indications. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delays in obtaining, or failures to obtain regulatory approvals would have a material adverse effect on our business. Marketing our products abroad will require similar regulatory approvals and is subject to similar risks. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Any products manufactured or distributed by us pursuant to FDA clearances or approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMPs, which impose procedural and documentation requirements upon us and our third party manufacturers. We cannot be certain that we, or our present or future suppliers, will be able to comply with the cGMP regulations and other FDA regulatory requirements. Failure to comply with these requirements can result in, among other things, total or partial suspension of production, failure of the government to grant approval for marketing, and withdrawal, suspension, or revocation of marketing approvals.

Once the FDA approves a product, a manufacturer must provide certain updated safety and efficacy information. Product changes, as well as certain changes in a manufacturing process or facility or other post-approval changes may necessitate additional FDA review and approval.

The FDA regulates drug labeling and promotion activities. The FDA has actively enforced regulations prohibiting the marketing of products for unapproved uses. Violations of the Federal Food, Drug, and Cosmetic Act or regulatory requirements may result in agency enforcement action, including voluntary or mandatory recall, suspension or revocation of product approval, product seizure, fines, injunctions or civil or criminal penalties. Our product development and testing activities are also subject to a variety of state laws and regulations. Any applicable state or local regulations may hinder our ability to manufacture or test our products in those states or localities. We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

The FDA's policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our potential products. Moreover, increased attention to the containment of health care costs in the United States and in foreign markets could result in new government regulations that could have a material adverse effect on our business. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

Foreign Regulatory Approval

Outside the United States, our ability to market our products will also be contingent upon receiving marketing authorizations from the appropriate regulatory authorities. The foreign regulatory approval process includes all the risks associated with FDA approval described above. The requirements governing conduct of clinical trials and marketing authorization vary widely from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure

provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

We plan to choose the appropriate route of European regulatory filing in an attempt to accomplish the most rapid regulatory approvals. However, the chosen regulatory strategy may not secure regulatory approvals or approvals of the chosen product indications. In addition, these approvals, if obtained, may take longer than anticipated. We cannot assure you that any of our product candidates will prove to be safe or effective, will receive regulatory approvals, or will be successfully commercialized.

Competition

The pharmaceutical and biotechnology industries in which we operate are characterized by rapidly advancing technologies, intense competition and an emphasis on proprietary products. Our competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. All of these competitors currently engage in, have engaged in or may engage in the future in the development, manufacturing, marketing and commercialization of new pharmaceuticals and pharmaceuticals, some of which may compete with our present or future product candidates.

We expect that our product candidates, if approved for marketing, will compete with existing drugs, therapies, drug delivery systems and technological approaches, as well as new drugs, therapies, drug delivery systems or technological approaches that may be developed or commercialized in the future. Any of these drugs, therapies, systems or approaches may receive government approval or gain market acceptance more rapidly than our product candidates, may offer therapeutic or cost advantages over our product candidates or may cure our targeted diseases or their underlying causes completely. As a result, our product candidates may become noncompetitive or obsolete.

AI-700, our ultrasound contrast agent for the assessment of myocardial perfusion, if approved for marketing and sale, will face intense competition. We believe that ultrasound with AI-700 can be a cost-effective and convenient substitute for nuclear stress tests, the current standard of care in myocardial perfusion assessment. In addition, we believe AI-700 will add useful myocardial perfusion information that stress echo cannot provide without a contrast agent. AI-700 is designed for use with widely available ultrasound equipment and techniques currently used for wall motion studies using stress echo. We expect to face intense competition from companies that market products related to these existing imaging techniques, as well as other companies that are developing ultrasound contrast agents for use in stress echo.

Nuclear stress testing is an established technique for assessing myocardial perfusion. Radioactive contrast agents that are approved by the FDA for use in nuclear stress tests include Cardiolite, which is marketed by Bristol-Myers Squibb Company; Myoview, which is marketed by Amersham plc; and thallium, which is marketed by Amersham, Bristol-Myers Squibb and Tyco International.

Stress echo without ultrasound contrast is an established technique for detecting abnormal wall motion, which some cardiologists may find satisfactory for the detection of coronary artery disease. However, stress echo without contrast is incapable of assessing myocardial perfusion. We believe that ultrasound with AI-700 will enable stress echo to provide information on myocardial perfusion in addition to wall motion.

No ultrasound contrast agent has been approved by the FDA for use in myocardial perfusion imaging or stress echo. However, we are aware of other companies that are or may be developing ultrasound contrast agents for use in stress echo. CardioSphere, which is being developed by Point Biomedical Corporation, is an ultrasound contrast agent for the assessment of myocardial perfusion. In March 2004, Point announced that it had recently completed two pivotal Phase III trials and plans to file an NDA with the FDA later this year. In addition, some companies have ultrasound contrast agents that are FDA

approved for resting wall motion studies or are in development. In the future, these companies may seek to broaden their indications to include stress echo and myocardial perfusion assessment. These FDA-approved agents include Optison, which is marketed by Amersham; Definity, which is marketed by Bristol-Myers Squibb; and Imagent, which is marketed by Imcor (formerly Photogen Technologies). SonoVue, which is being developed by Bracco, is an ultrasound contrast agent which we believe is in late stage clinical development for detecting abnormal wall motion and for radiology applications, but as of the date of this Annual Report has not received final approval from the FDA.

AI-850, our reformulation of paclitaxel, if approved for marketing and sale, will also face intense competition. We are aware of companies, such as American Pharmaceutical Partners, NeoPharm and Sonus Pharmaceuticals that are applying significant resources and expertise to developing reformulations of paclitaxel for intravenous delivery that will compete with our current product candidate. None of these reformulations have received final approval from the FDA. Other companies, such as Cell Therapeutics, are developing new chemical entities that involve paclitaxel conjugated, or chemically bound, to another chemical. None of these new chemical entities have received final approval from the FDA. In addition, a number of companies have developed technology for delivering hydrophobic drugs. Cardinal Health, CyDex and Elan have created formulations of hydrophobic drugs that have been approved by the FDA.

AI-128, our initial sustained release formulation of an asthma drug, if approved for marketing and sale, will also face intense competition. Companies such as Alkermes possess technology that may be suitable for sustained release pulmonary drug delivery and may have competitive programs that have not been publicly announced or may decide to begin such programs in the future. We are not aware of any other company currently in human clinical development of a sustained release version of the asthma drug that is currently the subject of our research and development efforts. In addition, many asthma drugs are marketed by large pharmaceutical companies with much greater resources than us. These companies may be developing sustained release versions of their asthma drugs that would compete with our sustained release product candidate.

Many of our competitors in these markets have greater development, financial, manufacturing, marketing, and sales experience and resources than we do and we cannot be certain that they will not succeed in developing products or technologies which will render our technologies and products obsolete or noncompetitive. We cannot assure you that our products will compete successfully with these newly emerging technologies. In addition, many of those competitors have significantly greater experience than we do in their respective fields. Many of these competitors may have greater name recognition than we do, and may offer discounts as a competitive tactic.

Employees

As of March 1, 2004, we had 58 full-time employees, including 48 in research and development and 10 in general and administrative. Ten of our employees had M.D.s and/or Ph.D.s. From time to time, we also employ independent contractors to support our engineering and administrative organizations. None of our employees are represented by a collective bargaining unit and we have never experienced a work stoppage. We consider our relations with our employees to be good.

Organization and Trademarks

We were organized as a Delaware corporation on July 12, 1993.

We have trademarks in the United States and other countries, including "Acusphere," "HDDS" and "PDDS" and our logo. This Annual Report on Form 10-K also contains the trademarks and tradenames of other entities that are the property of their respective owners.

Item 2. ***Properties***

Our offices and laboratory facilities are located in one 47,500 square foot facility located in Watertown, Massachusetts. We lease the space in this facility under a ten year operating lease that expires in December 2011. We conduct our clinical manufacturing through a contract manufacturer that is experienced in producing clinical material. A portion of our 47,500 square foot facility has not been internally built-out pending our demand for the space. We intend to improve and use this space when needed. We anticipate that this currently unused space will in the coming years be needed to expand our internal laboratory and pilot-manufacturing capabilities. We believe that our existing facility is adequate to meet our current and foreseeable requirements and that suitable additional space will be available as needed. If we decide not to use third-party contract manufactures for production of commercial quantities of AI-700, additional space may be required beginning in 2004.

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***

None.

PART II

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

Price Range of Common Stock

Our common stock has been traded on the Nasdaq National Market under the symbol "ACUS" since October 8, 2004. Prior to that time, there was no public market for the common stock. The following table sets forth the range of high and low closing sale prices for the common stock as reported on the Nasdaq National Market during the fourth quarter of 2003.

	High	Low
Year ended December 31, 2003:		
Fourth quarter (commencing with our first day of trading on October 8, 2003)	$14.03	$6.99

On March 1, 2004, the last reported sale price of the Common Stock on The Nasdaq National Market was $8.66 per share. As of March 1, 2004, there were approximately 938 holders of record of the Common Stock, including multiple beneficial holders at depositories, banks and brokers included as a single holder in the single "street" name of each respective depository, bank or broker.

Dividend Policy

We have never declared or paid a cash dividend on our capital stock. We currently intend to retain any earnings for use in our business and do not anticipate paying any cash dividends on our capital stock in the foreseeable future.

Equity Compensation Plan Information

See Part III, Item 12 for information regarding securities authorized for issuance under our equity compensation plans.

Recent Sales of Securities

In April 2003, we issued and sold 10% convertible promissory notes in the principal amount of $19,100,000 in a private placement to 23 investors. In June 2003, we issued and sold 10% convertible

promissory notes in the principal amount of $319,000 in a private placement to 6 investors. The convertible promissory notes bore interest at a rate of 10% per annum. The outstanding balance of the convertible promissory notes and accrued interest thereon converted into 2,411,846 shares of our common stock upon the closing of our initial public offering. Concurrent with the issuance of these promissory notes, we issued for no additional consideration warrants to purchase 458,437 shares of our common stock at an exercise price of $8.46 per share, and a warrant to purchase 684 shares of our common stock at an exercise price of $14.00 per share. Warrants to purchase 451,581 shares of our common stock are exercisable at the election of the holder on or prior to the earlier of a change of control of the Company and April 11, 2008, and warrants to purchase 7,540 shares of our common stock are exercisable at the election of the holder on or prior to a change of control of the Company and June 27, 2008. These securities were issued to accredited investors in a private placement transaction exempt from registration pursuant to Section 4(2) of the Securities Act of 1933 and Rule 506 of Regulation D as an issuer transaction not involving a public offering.

During the quarter ended December 31, 2003, we granted options to purchase an aggregate of 17,000 shares of our common stock to employees under our 1994 Stock Plan, at a weighted average exercise price of $7.30 per share. In addition, we issued 1,167 shares of common stock during the quarter ended December 31, 2003 in connection with the exercise of outstanding options under our 1994 Stock Plan by one of our employees, at a weighted exercise price of $0.96 per share. These option exercises resulted in aggregate proceeds to us of approximately $1,120.

No underwriters were involved in the foregoing stock or option issuances. The foregoing stock and option issuances were exempt from registration under the Securities Act of 1933, as amended, either pursuant to Rule 701 under the Act, as transactions pursuant to a compensatory benefit plan, or pursuant to Section 4(2) under the Act, as a transaction by an issuer not involving a public offering.

On October 14, 2003, we closed the sale of an aggregate of 3,750,000 shares of our common stock, $0.01 par value, in our initial public offering at a price to the public of $14.00 per share. The managing underwriters in the offering were SG Cowen Securities Corporation, Thomas Weisel Partners LLC, U.S. Bancorp Piper Jaffray and Friedman Billings Ramsey. All of the shares of common stock sold in the offering were registered under the 1933 Act on a Registration Statement on Form S-1 (Reg. No. 333-106725) that was declared effective by the SEC on October 7, 2003 and a Registration Statement filed pursuant to Rule 424(b) under the Securities Act that was filed on October 8, 2003 (Reg. No. 333-106725). The offering commenced on October 7, 2003 and did not terminate until after the sale of all of the securities registered in the Registration Statement. As part of the initial public offering, we granted the several underwriters an overallotment option to purchase up to an additional 562,500 shares of our common stock from us. The underwriters did not exercise the overallotment option. There were no selling stockholders in the offering.

The aggregate price of the offering amount registered on our behalf was $52.5 million. In connection with the offering, we paid $3.7 million in underwriting discounts and commissions to the underwriters and incurred an estimated $1.2 million in other offering expenses. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours. After deducting the underwriting discounts and commissions and offering expenses, we received net proceeds from the offering of approximately $47.6 million.

We anticipate using the net proceeds from the offering for research and development activities, including clinical trials for our lead product candidate, working capital and other general corporate purposes. Pending such uses, we have invested the net proceeds from the offering in short-term, interest bearing investment grade securities. The amount and timing of our actual expenditures will depend on numerous factors, including the progress of our research and development activities and clinical trials, the number and breadth of our product development programs, our ability to establish and maintain corporate collaborations and other arrangements and the amount of cash, if any, generated by our operations. In addition, a portion of the net proceeds may be used for the acquisition of businesses, products and

technologies that are complementary to our own, although we currently do not have any understandings, commitments or agreements with respect to acquisitions. We retain broad discretion in the allocation and use of the net proceeds.

Item 6. *Selected Financial Data*

The selected financial data set forth below has been derived from our audited financial statements. This information should be read in conjunction with the financial statements and the related notes thereto, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other financial information included elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,				
	1999	2000	2001	2002	2003
	(In thousands, except per share data)				
Statement of Operations Data:					
Operating Expenses:					
Research and development	$ 7,022	$ 9,978	$ 11,536	$ 13,545	$ 14,228
General and administrative	1,622	2,517	3,893	3,906	4,173
Stock-based compensation	5	16	1,076	2,195	1,307
Total operating expenses	8,649	12,511	16,505	19,646	19,708
Equity in loss of joint venture	—	(12,015)	(1,965)	(1,183)	—
Interest and other income (expense), net	(492)	97	193	(1,067)	(2,215)
Net loss	(9,141)	(24,429)	(18,277)	(21,896)	(21,923)
Accretion of dividends and offering costs on preferred stock	(2,604)	(4,218)	(6,249)	(6,666)	(5,948)
Net loss available to common stockholders	$(11,745)	$(28,647)	$(24,526)	$(28,562)	$(27,871)
Net loss available to common stockholders per share — Basic and diluted	$ (27.24)	$ (64.18)	$ (50.81)	$ (35.39)	$ (6.66)
Weighted average shares outstanding — Basic and diluted	432	446	483	807	4,188

	As of December 31,				
	1999	2000	2001	2002	2003
	(In thousands, except per share data)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 2,230	$ 25,275	$ 15,599	$ 7,992	$54,562
Working capital	(1,498)	18,457	10,749	2,899	50,931
Total assets	5,104	29,092	24,457	13,367	58,924
Long-term debt, net of current portion	4,288	1,104	5,290	1,726	205
Redeemable convertible preferred stock	32,540	85,009	97,739	91,467	—
Total stockholders' (deficit) equity	(35,482)	(64,030)	(86,228)	(85,348)	54,375

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

Statements in the following discussion contain certain projections, estimates and other forward-looking statements. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Our actual results and the timing of certain events may differ materially from the results discussed, projected, anticipated or indicated in any forward-looking statement. Any forward-looking statement should be considered in light of factors discussed in Item 7 under "Certain Factors Which May Affect Future Results" and elsewhere in this Annual Report on Form 10-K. We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

The following discussion should be read in conjunction with our consolidated financial statements and related notes thereto included elsewhere in this Annual Report on Form 10-K.

Overview

We are a specialty pharmaceutical company that develops new drugs and improved formulations of existing drugs using our proprietary porous microparticle technology. We are focused on developing proprietary drugs that can offer significant benefits such as improved safety and efficacy, increased patient compliance, greater ease of use, expanded indications or reduced cost. Our three initial product candidates are in clinical development and are designed to address large unmet clinical needs within cardiology, oncology and asthma. Our lead product candidate is a cardiovascular drug in Phase III clinical development for the detection of coronary artery disease, the leading cause of death in the United States.

We created our three initial product candidates using technology that enables us to control the size and porosity of particles in a versatile manner, so we can customize the particles to address the delivery needs of a variety of drugs. We are focused on creating porous microparticles that are smaller than red blood cells. Some of these microparticles are nanoparticles which are smaller than 1 micron. Small microparticles are important for delivering drugs intravenously so that they can pass through the body's smallest blood vessels, for increasing the surface area of a drug so that the drug will dissolve more rapidly, and for delivering drugs to the lung via inhalation. Porosity is important for entrapping gases in microparticles, for controlling the release rate of the drug from a microparticle, and for targeting inhaled drugs to specific regions of the lung.

We are a development stage company and have devoted substantially all of our efforts towards the research and development of our product candidates and raising capital. Since our inception, we have had no revenue from product sales and have funded our operations almost exclusively through the private and public placement of equity securities, equipment leases and debt financings. We have not been profitable and have incurred a cumulative net loss of $115.2 million from inception through December 31, 2003.

We expect to incur significant operating losses for the next several years. Research and development expenses relating to our product candidates will continue to increase. In particular, we expect to incur increased costs for Phase III clinical trials of AI-700. General and administrative costs will increase as we prepare for the commercialization of our product candidates and as we incur costs associated with operating as a newly public company. Manufacturing expenses, which are currently part of research and development expenses, will also increase as we prepare for the commercialization of our product candidates.

Financial Operations Overview

Revenues. We have not generated any operating revenues since our inception and do not expect operating revenues in the near future. Further in the future, we will seek to generate revenues from a

combination of product sales, up-front or milestone payments in connection with collaborative or strategic relationships, and royalties resulting from the license of our intellectual property.

Research and Development Expense. Research and development expense consists of expenses incurred in developing and testing product candidates. These expenses consist primarily of salaries and related expenses for personnel, fees paid to professional service providers in conjunction with independently monitoring our clinical trials and acquiring and evaluating data in conjunction with our clinical trials, costs of contract manufacturing services, costs of materials used in clinical trials and research and development, depreciation of capital resources used to develop our products, costs of facilities and the legal costs of pursuing patent protection on select elements of our intellectual property. We expense research and development costs, including patent related costs, as incurred. We believe that significant investment in product development is a competitive necessity and plan to continue these investments in order to realize the potential of our product candidates and proprietary technologies. Development programs for later stage product candidates, such as AI-700, tend to cost more than earlier stage programs due to the length and the number of patients enrolled in clinical trials for later stage programs. From inception through December 31, 2003, we cumulatively spent $72.6 million on research and development. Additionally, from June 2000 through September 2002, we performed research and development through a joint venture, as discussed below.

General and Administrative Expense. General and administrative expense consists primarily of salaries and other related costs for personnel in executive, finance, accounting, information technology and human resource functions. Other costs include facility costs not otherwise included in research and development expense and professional fees for legal and accounting services. From inception through December 31, 2003, we have cumulatively incurred $20.1 million in general and administrative expense.

Stock-Based Compensation Expense. Stock-based compensation expense, which is a non-cash charge, results principally from stock option grants to our employees at exercise prices deemed for accounting purposes to be below the fair market value of our stock on the date the stock options were granted ("fixed awards"). We have granted stock options for which the exercise prices were deemed for accounting purposes to be below the fair value of the underlying common stock resulting in our recording stock-based compensation expense associated with such grants. Stock-based compensation expense is also recorded for stock option grants to non-employees and for restricted stock grants provided to directors and advisors in lieu of cash compensation. Deferred compensation on fixed awards is amortized as a charge to operations over the vesting periods of the options and grants, subject to adjustment for forfeiture during the vesting period. As of December 31, 2003, we deferred $1.7 million in stock-based compensation and, from inception through December 31, 2003, recognized stock-based compensation expense of $4.7 million.

Equity in Loss of Joint Venture. In June 2000, we established in collaboration with Elan Corporation, plc and its affiliates a joint venture, Acusphere Newco, Ltd., a Bermuda corporation, to develop and commercialize pulmonary drug delivery product candidates. In September 2002, we reached an agreement with Elan terminating the joint venture in a cash-free transaction. Equity in loss of joint venture consists of our portion of the losses from Acusphere Newco, Ltd. from June 2000, when the joint venture was established, until September 2002, when the joint venture was terminated. During that period, we owned an 80.1% interest in the joint venture and Elan owned a 19.9% interest in the joint venture on a fully diluted basis. Elan had retained significant minority investor rights that prevented us from exercising full control over the joint venture. Accordingly, during the period from June 2000 to September 2002, we recorded net losses of the joint venture in accordance with our percentage ownership (80.1%) of such entity and reported such loss using the equity method of accounting. In connection with the termination of the joint venture we recorded a loss of $381,413 for an amount previously recorded as due from Elan. Including this amount, from inception through the date on which we terminated our joint venture with Elan, we cumulatively incurred $15.2 million in equity in loss of joint venture.

Interest and Other Income (Expense). Interest income consists of interest earned on our cash, cash equivalents and short-term investments. Interest expense consists of interest incurred on equipment leases and on debt financings.

Accretion of Dividends and Offering Costs on Convertible Preferred Stock. Accretion of dividends and offering costs on convertible preferred stock primarily consists of dividends on convertible preferred stock. Prior to conversion of convertible preferred stock to common stock, which occurred on October 14, 2003 upon the completion of the Company's initial public offering, our convertible preferred stock was entitled to accretion of dividends, the amount of which decreased the amount of stockholders' equity available to common stockholders and effectively increases the loss per share of common stock. After October 14, 2003, no existing convertible preferred stock is outstanding, and accordingly there will be no further accretion of dividends and offering costs on these shares. All preferred stock dividends which were accreted before October 14, 2003 were per agreement forfeited by the preferred stockholders on that date in connection with the conversion of these preferred shares to common stock.

Results of Operations

Years Ended December 31, 2001, 2002 and 2003

Research and Development Expense. Research and development expense for the year ended December 31, 2003 was $14.2 million, compared to $13.5 million in 2002 and $11.5 million in 2001. The $684,000 increase in 2003 over 2002 represented an increase of 5% and the $2.0 million increase in 2002 over 2001 represented an increase of 17%.

In 2003 compared to 2002, the higher research and development expense primarily resulted from costs associated with the start of our Phase III clinical program for AI-700, including increased costs associated with clinical site training and clinical site monitoring. In 2002 compared to 2001, our increased research and development expense primarily resulted from increased facility costs and increased pulmonary drug development costs, net of costs attributable to the Elan joint venture.

The following table summarizes the primary components of our research and development expense for the years ended December 31, 2001, 2002 and 2003. Because of our ability to utilize resources across several projects, many of our research and development costs are not tied to any individual project and are allocated among multiple projects. We record direct costs on a project-by-project basis. We record indirect costs in aggregate in support of all research and development.

	Years Ended December 31,		
	2001	2002	2003
		(In thousands)	
AI-700	$ 5,209	$ 5,332	$ 8,560
AI-850 and AI-128	3,481	2,992	777
Other	98	1,490	1,305
Total direct costs	8,788	9,814	10,642
Facility costs	1,093	2,106	1,962
Depreciation	1,280	1,363	1,299
Patent costs	375	262	325
Total research and development expense	$11,536	$13,545	$14,228

Research and development costs generally increase as programs progress from early stage clinical trials to late stage clinical trials. Our primary research and development programs are as follows:

- *Late Stage Clinical Development Program (AI-700).* Our lead product candidate, AI-700, is a cardiovascular drug for the detection of coronary artery disease. We incurred direct research and development expense for AI-700 in 2003 of $8.6 million, $5.3 million in 2002 and in 2001 of $5.2 million. Of these amounts, $1.7 million in 2003, $1.6 million in 2002 and $1.4 million in 2001 were incurred in connection with the production of clinical trial material by a third-party contract manufacturer. In 2003, we commenced clinical studies in our Phase III clinical program for AI-700, and we identified and began training additional clinical sites to be part of this Phase III

clinical program. We anticipate that new clinical sites for this clinical trial, in both Europe and North America, will be trained and initiated during 2004. As clinical sites are initiated and increasing numbers of patients are enrolled in the Phase III clinical program, we anticipate incurring increased costs from professional service firms helping to support the clinical trial by providing services such as independent clinical monitoring, data acquisition and data evaluation. We also anticipate incurring increased costs related to hiring of additional research and development and clinical personnel. In addition, we anticipate incurring increased costs associated with production and distribution of clinical trial material, including production in 2004 of clinical trial material which meets our requirements for the pivotal trials of our Phase III clinical program, and with preparation for commercial production.

- *Early Stage Clinical Development Programs (AI-850 and AI-128).* Our initial clinical applications of our HDDS technology, AI-850, and our PDDS technology, AI-128, are in early stages of clinical development. We incurred direct research and development expense for AI-850 and AI-128 in 2003 of $777,000, $3.0 million in 2002 and in 2001 of $3.5 million. Of these amounts, $781,000 in 2002 and $231,000 in 2001 was incurred in connection with the production of clinical trial material by a third-party contract manufacturer. There were no contract manufacturing costs incurred in connection with these product development programs in 2003. These amounts exclude direct costs of $731,000 and $1.6 million incurred in 2002 and 2001 for pulmonary drug development through the Elan joint venture, which was terminated in September 2002. We anticipate that we will complete our Phase I study of AI-850 in 2004 and that our costs associated with these clinical programs will not increase until we are prepared to commence further pre-clinical and clinical testing using our own resources or through strategic collaborations.

- *Other.* Other direct research and development costs primarily consist of management and preclinical evaluation of other product candidates.

Each of our research and development programs is subject to risks and uncertainties, including the requirement to seek regulatory approvals, which are outside of our control. For example, our clinical trials may be subject to delays or rejections based on our inability to enroll patients at the rate that we expect or our inability to produce clinical trial material in sufficient quantities and of sufficient quality to meet the schedule for our planned clinical trials. Moreover, the product candidates identified in these research and development programs, particularly our early stage programs, must overcome significant technological, manufacturing and marketing challenges before they can be successfully commercialized. As a result of these risks and uncertainties, we are unable to predict with any certainty the period in which material net cash inflows from such projects could be expected to commence or the completion date of these programs. Failure to commercialize these product candidates on a timely basis could have a material adverse affect on our business, financial condition and results of operations. We may seek to establish collaborative relationships to help us commercialize these product candidates, but there can be no assurance that we will be successful in doing so.

General and Administrative Expense. General and administrative expense for the year ended December 31, 2003 was $4.2 million, compared to $3.9 million for 2002 and $3.9 million in 2001. The $267,000 increase in 2003 over 2002 represented an increase of 7% while the activity from between 2002 and 2001 remained stable.

In 2003 compared to 2002, the increase in general and administrative expense primarily resulted from hiring experienced personnel in both the finance and business development areas. This increase also includes legal and other support costs associated with operating as a public company.

In 2002 compared to 2001, general and administrative expense included increased office rent costs of $239,000, increased payroll and benefit costs of $183,000 and increases in various other costs of lesser individual amounts. These increases were substantially offset by decreased legal, accounting and printing costs of $623,000.

We anticipate some overall increase in general and administrative expense, including increases in costs for investor relations and other activities associated with operating as a publicly-traded company. These increases will also likely include the hiring of additional personnel. We intend to continue to incur various internal and external business development costs to support our various product development efforts, and certain of these expenses are likely to increase overall. However, until we are closer to substantially completing enrollment of the majority of patients required in the AI-700 Phase III clinical program, we do not anticipate incurring significantly increased costs to accelerate preparations for the commercial introduction of AI-700.

Stock-Based Compensation Expense. Stock-based compensation expense for the year ended December 31, 2003 was $1.3 million, compared to $2.2 million in 2002 and $1.1 million in 2001. The $888,000 decrease in 2003 over 2002 represented a decrease of 40% and the $1.1 million increase in 2002 over 2001 represented an increase of 104%. The variances between the years resulted principally from the timing of the expense of the deferred stock-based compensation for stock options granted in prior years.

Equity in Loss of Joint Venture. Our joint venture with Elan was terminated in September 2002. During the year ended December 31, 2002, we recognized a $1.2 million loss from our 80.1% equity share in the loss of the Elan joint venture. This amount related to research and development of pulmonary drug delivery product candidates and from the expense of an amount previously recorded as due from Elan. Research and development costs for pulmonary drug delivery product candidates in 2003 are included in research and development expense, as discussed above.

Interest and Other Income (Expense). Interest and other income (expense) for the year ended December 31, 2003 was $2.2 million of net expense, compared to $1.1 million of net expense in 2002 and $193,000 net interest income in 2001. The $1.1 million increase in net expense in 2003 over 2002 represented an increase of 108% and the $1.3 million increase in net expense in 2002 over 2001 represented an increase of 652%. During these periods, interest and other income (expense) consisted of the following:

	Year Ended December 31,		
	2001	2002	2003
Interest income	$ 943,000	$ 224,000	$ 200,000
Other income (expense)	—	9,000	22,000
Interest expense	(750,000)	(1,300,000)	(2,437,000)
Total, net	$ 193,000	$(1,067,000)	$(2,215,000)

The decrease in interest income for the year ended December 31,2003 compared to the year ended December 31, 2002 was primarily due to reduced yields on investments. The increase in interest expense for the year ended December 31, 2003 compared to the year ended December 31, 2002 was primarily due to $762,000 of costs incurred from the amortization of the discount recorded for accounting purposes on the warrants issued in connection with the 10% convertible promissory notes in April and June 2003 and to $984,000 of interest accrued on the 10% convertible promissory notes, partially offset by a decrease of $461,000 in interest paid on the subordinated loans payable and the decrease of $153,000 in amortization of the warrants issued in connection with the subordinated loans payable, due to the early repayment in 2003 of these subordinated loans payable.

The decrease in interest income the year ended December 31, 2002 compared to the year ended December 31, 2001 resulted principally from reduced yields on investments resulting from lower average interest rates and to lower average fund balance available for investment. The increase in interest expense in 2002 compared to 2001 primarily resulted from the amortization of the fair value of warrants issued in September 2001 in connection with subordinated loans payable.

Accretion of Dividends and Offering Costs on Convertible Preferred Stock. Accretion of dividends and offering costs on convertible preferred stock was $5.9 million in 2003, $6.7 million in 2002 and

$6.2 million in 2001. The $717,000 decrease in 2003 over 2002 represented a decrease of 11% and the $417,000 increase in 2002 over 2001 represented an increase of 7%.

In 2003 compared to 2002, the decrease in accretion of dividends and offering costs resulted primarily from the conversion of convertible preferred stock into common stock in conjunction with the Company's initial public offering in October 2003. After October 14, 2003, no convertible preferred stock remains outstanding and, accordingly, there was no further accretion of dividends and offering costs on these shares after that date. In connection with the conversion of preferred stock to common stock, all previously accreted dividends on the convertible preferred stock were forfeited by the holders.

In 2002 compared to 2001, the increase in accretion of dividends and offering costs reflected the increase in accretion of dividends on convertible preferred stock issued in June 2002, the Series J convertible preferred stock, and in June 2001, the Series I convertible preferred stock.

Liquidity and Capital Resources

Historically, we have financed our business through the issuance of equity securities, debt financings and equipment leases. Our liquidity requirements have arisen primarily from research and development expenditures, equipment expenditures and payments on outstanding indebtedness. As of December 31, 2003, we had cash, cash equivalents and short-term investments of $54.6 million. Since our inception in July 1993 through December 31, 2003, we have raised $161.6 million through the issuance of equity securities, including the Company's initial public offering on October 14, 2003 and the $19.4 million in convertible promissory notes which converted to common stock upon the Company's initial public offering. As of December 31, 2003 we owed $1.1 million from capital leases and had commitments totaling $19.4 million for rent under our facility lease.

On October 14, 2003 we closed our initial public offering at a price to the public of $14.00 per share. We sold 3,750,000 shares of our common stock in the offering and the aggregate price of the offering registered on our behalf was $52.5 million. In connection with the offering, we paid $3.7 million in underwriting discounts and commissions to underwriters and incurred approximately $1.2 million in other offering expenses. After deducting the underwriting discounts and commissions and estimated offering expenses, we received net proceeds from the offering of approximately $47.6 million.

On April 11, 2003 and June 27, 2003, we raised $19.1 million and $319,000, respectively, from existing preferred stockholders in exchange for 10% convertible promissory notes and warrants. Upon completion of our initial public offering on October 14, 2003, the 10% convertible promissory notes and interest accrued thereon converted into 2,411,846 shares of common stock.

During the year ended December 31, 2003, operating activities used $15.5 million of cash. Net cash used by operating activities during this period resulted primarily from a net loss of $21.9 million. This use of cash was partially offset by increases in accrued expenses of $1.7 million, increases in accounts payable of $782,000, non-cash charges for depreciation and amortization of $1.7 million, non-cash charges for stock-based compensation expense of $1.3 and non-cash interest expense of $1.1 million.

During the year ended December 31, 2003, investing activities used $459,000 in cash. Purchases of equipment used $535,000 and an increase in other assets of $119,000, partially offset by maturities (purchases) of short term investments of $195,000.

During the year ended December 31, 2003, financing activities provided $62.7 million in cash, with proceeds of $47.6 million from the Company's initial public offering, $19.4 million from the issuance of 10% convertible promissory notes which were partially offset by $4.4 million for scheduled and early repayment of debt.

We believe, based on our operating plans, that the proceeds of our initial public offering that closed October 14, 2003 together with our existing resources will be sufficient to fund our planned operations, including increases in spending for our AI-700 Phase III clinical program, for at least the next twelve months. However, over the next several years we may require significant additional funds to develop,

conduct clinical trials, achieve regulatory approvals and, subject to regulatory approval, commercially launch AI-700, our other product candidates under development and future product candidates. Our future capital requirements will depend on many factors, including the scope and progress made in our research and development activities and our clinical trials. We may also need additional funds for possible future strategic acquisitions of businesses, products or technologies complementary to our business. We do not expect to generate significant revenues, other than possible license or milestone payments, from commercial sale of our products unless or until we or potential partners complete clinical trials for our products and receive marketing approval from the applicable regulatory authorities. If additional funds are required, we may raise such funds from time to time through public or private sales of equity or from borrowings. Financing may not be available on acceptable terms, or at all, and our failure to raise capital when needed could materially adversely impact our growth plans and our financial condition and results of operations. Additional equity financing may be dilutive to the holders of our common stock and debt financing, if available, may involve significant cash payment obligations and covenants that restrict our ability to operate our business.

Off-Balance Sheet Financing Arrangements

We currently do not have any special purpose entities or off-balance sheet financing arrangements.

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2003 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

Payments Due by Period

	Total Obligations All Years	2004 Through 2005	2006 Through 2007	2008 Through 2009	After 2009
			(In thousands)		
Capital lease obligations	$ 1,090	$1,090	$ —	$ —	$ —
Operating lease obligations	19,419	4,366	4,677	5,010	5,367
Total contractual cash obligations	$20,509	$5,456	$4,677	$5,010	$5,367

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on 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, liabilities and expenses. On an on-going basis, we evaluate our estimates and judgments, including those related to accrued expenses, fair valuation of stock related to stock-based compensation and income taxes. We based our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe the following critical accounting policies affect our more significant judgments and estimates used in the preparation of our consolidated financial statements.

Accrued Expenses. As part of the process of preparing consolidated financial statements we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our consolidated financial statements. Examples of estimated expenses for which we accrue include professional service fees, such as lawyers and accountants, and

contract service fees such as amounts paid to clinical monitors, data management organizations and investigators in conjunction with clinical trials, and fees paid to contract manufacturers in conjunction with the production of clinical materials. In connection with such service fees, our estimates are most affected by our understanding of the status and timing of services provided relative to the actual levels of services incurred by such service providers. The majority of our service providers invoice us monthly in arrears for services performed. In the event that we do not identify certain costs which have begun to be incurred or we under- or over-estimate the level of services performed or the costs of such services, our reported expenses for such period would be too low or too high. The date on which certain services commence, the level of services performed on or before a given date and the cost of such services are often judgmental. We make these judgments based upon the facts and circumstances known to us in accordance with generally accepted accounting principles.

Stock-Based Compensation and Other Equity Instruments. We have elected to follow APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations, in accounting for our stock-based compensation plans, rather than the alternative fair value accounting method provided for under SFAS No. 123, *Accounting for Stock-Based Compensation*. Accordingly, we have not recorded stock-based compensation expense for stock options issued to employees in fixed amounts with exercise prices at least equal to the fair value of the underlying common stock on the date of grant. In the notes to our consolidated financial statements we provide pro forma disclosures in accordance with SFAS No. 123 and related pronouncements. We account for transactions in which services are received in exchange for equity instruments based on the fair value of such services received from non-employees or of the equity instruments issued, whichever is more reliably measured, in accordance with SFAS No. 123 and EITF Issue No. 96-18, *Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*. We account for transactions in which we grant warrants in connection with the issuance of debt in accordance with APB 14, *Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants*. The two factors which most affect charges or credits to operations related to stock-based compensation are the fair value of the common stock underlying stock options for which stock-based compensation is recorded and the volatility of such fair value.

Accounting for equity instruments granted or sold by us under APB No. 14, APB No. 25, SFAS No. 123 and EITF No. 96-18 requires fair value estimates of the equity instrument granted or sold. If our estimates of the fair value of these equity instruments are too high or too low, it would have the effect of overstating or understating expenses. When equity instruments are granted or sold in exchange for the receipt of goods or services and the value of those goods or services can be readily estimated, we use the value of such goods or services to determine the fair value of the equity instruments. When equity instruments are granted or sold in exchange for the receipt of goods or services and the value of those goods or services can not be readily estimated, as is true in connection with most stock options and warrants granted to employees or non-employees, we estimated the fair value of the equity instruments based upon consideration of factors which we deemed to be relevant at the time using cost, market and/or income approaches to such valuations. Because shares of our common stock were not publicly traded prior to our initial public offering in October 2003, market factors historically considered in valuing stock and stock option grants include comparative values of public companies discounted for the risk and limited liquidity provided for in the shares we are issuing, pricing of private sales of our convertible preferred stock, prior valuations of stock grants and the effect of events that have occurred between the time of such grants, economic trends, perspective provided by investment banks and the comparative rights and preferences of the security being granted compared to the rights and preferences of our other outstanding equity.

Income Taxes. As part of the process of preparing our consolidated financial statements we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves us estimating our actual current tax exposure together with assessing temporary differences resulting from differing treatments of items for tax and accounting purposes. These differences result in deferred tax assets and liabilities. In addition, as of December 31, 2003, we had federal tax net operating

loss carryforwards of $68.5 million, which expire through 2023. We also have research and development credit carryforwards of $2.6 million. We have recorded a valuation allowance to fully offset against these otherwise recognizable net deferred tax assets due to the uncertainty surrounding the timing of the realization of the tax benefit. In the event that we determine in the future that we will be able to realize all or a portion of its net deferred tax benefit, an adjustment to deferred tax valuation allowance would increase net income in the period in which such a determination is made. The Tax Reform Act of 1986 contains provisions that may limit the utilization of net operating loss carryforwards and credits available to be used in any given year in the event of significant changes in ownership interest, as defined.

Recently Issued Accounting Pronouncements

In January 2003, the Financial Accounting Standards Board issued Interpretation No. 46, "Consolidation of Variable Interest Entities" (FIN 46), which was amended by FIN 46R issued in December 2003. This interpretation of Accounting Research Bulletin No. 51, "Consolidated Financial Statements," addresses consolidation by business enterprises of variable interest entities (VIEs) that either: (1) do not have sufficient equity investment at risk to permit the entity to finance its activities without additional subordinated financial support, or (2) for which the equity investors lack an essential characteristic of a controlling financial interest. This Interpretation applies immediately to VIEs created after January 31, 2003. It also applies in the first fiscal year or interim period ending after March 15, 2004, to VIEs created before February 1, 2003 in which an enterprise holds a variable interest. FIN 46 requires disclosure of VIEs in financial statements issued after January 31, 2003, if it is reasonably possible that as of the transition date: (1) the company will be the primary beneficiary of an existing VIE that will require consolidation or, (2) the company will hold a significant variable interest in, or have significant involvement with, an existing VIE. We are currently in the process of completing our review of the requirements of FIN 46. However, we have not yet identified any entities that require disclosure or entities that would require consolidation under FIN 46 that had not previously been consolidated as a result of FIN 46.

Certain Factors Which May Affect Future Results

Our operating results and financial condition have varied in the past and may in the future vary significantly depending on a number of factors. Except for the historical information in this report, the matters contained in this report include forward-looking statements that involve risks and uncertainties. The following factors, among others, could cause actual results to differ materially from those contained in forward-looking statements made in this report and presented elsewhere by management from time to time. Such factors, among others, may have a material adverse effect upon our business, results of operations and financial condition.

Risks Related to Our Company

We have not generated revenues to date, and we may not achieve profitability for some time, if at all.

We are focused on product development and we have not generated any revenues to date. We have incurred losses each year of our operations and we expect to continue to incur operating losses for the next several years. The process of developing our products requires significant clinical, development and laboratory testing and clinical trials as well as regulatory approvals. In addition, commercialization of our product candidates will require us to establish sales, marketing and manufacturing capabilities, either through internal hiring or through contractual relationships with others. We expect our research and development and general and administrative expenses will increase over the next several years. As of December 31, 2003, our cumulative net loss was $115.2 million. Our net loss was $21.9 million for the full year 2002 and $21.9 million for the full year 2003.

If we fail to obtain regulatory approvals for our product candidates under development, and in particular our lead product candidate AI-700, we will not be able to generate revenues from the commercialization or sale of our product candidates.

We must receive regulatory approval of each of our product candidates before we can commercialize or sell that product candidate. The pre-clinical laboratory testing, formulation development, manufacturing and clinical trials of any product candidates we develop independently or in collaboration with third parties, as well as the distribution and marketing of these product candidates, are regulated by numerous federal, state and local governmental authorities in the United States, principally the FDA, and by similar agencies in other countries. The development and regulatory approval process takes many years, requires the expenditure of substantial resources, is uncertain and subject to delays, and will thus delay our receipt of revenues, if any, from any of our product candidates. We cannot assure you that our clinical trials will demonstrate the safety and efficacy of any of our product candidates or will result in marketable products.

No product can receive FDA approval unless human clinical trials show both safety and efficacy for each target indication in accordance with FDA standards. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in early stage development. We therefore cannot assure you that the results from our Phase II clinical trials for AI-700 will be predictive of results obtained in our Phase III clinical trials. Many of the patients in our AI-700 clinical trial have coronary heart disease. As part of our AI-700 Phase III clinical trials, patients will be exposed to potential safety risks associated with a stress test, including risks associated with a pharmacological stressor, and AI-700. Given the nature of the AI-700 Phase III clinical trial, including administering AI-700 to larger numbers of at-risk patients and new clinical sites, adverse events are expected to be encountered during the clinical trial. Adverse events are also likely to be encountered in clinical trials for our other products, which clinical trials also include at-risk patients. For example, our AI-850 trial consists of patients being treated for late-stage cancer. If significant adverse events are detected and these events are attributable to our products, such events could delay, limit or prevent regulatory agency approval. Further, data obtained from pre-clinical and clinical activities are subject to varying interpretations that could delay, limit or prevent regulatory agency approval. We cannot assure you that our Phase III plan for AI-700 will successfully address the concerns of the FDA or that the results of the Phase III program will establish the safety and efficacy of AI-700 sufficiently for us to obtain regulatory approval.

We may also encounter delays or rejections based on our inability to enroll enough patients to complete our clinical trials. Patient enrollment depends on many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, and the eligibility criteria for the study. Delays in planned patient enrollment may result in increased costs and delays, which could have a harmful effect on our ability to develop products. We may encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a drug or the period required for review of any application for regulatory agency approval of a particular compound. We also may encounter delays in the event we are unable to produce clinical trial material in sufficient quantities and of sufficient quality to meet the schedule for our planned clinical trials. In addition, we rely on a number of third parties, such as clinical research organizations, to help support the clinical trials by performing independent clinical monitoring, data acquisition and data evaluations. Any failure on the part of these third parties could delay the regulatory approval process.

Failure to obtain regulatory approval or any delay or setback in obtaining regulatory agency approvals could:

- adversely affect our ability to market any drugs we develop independently or with collaborative partners;
- impose additional costs and diminish any competitive advantages that we may attain; or
- adversely affect our ability to generate royalties.

In particular, failure to obtain approval or substantial delays in obtaining approval for our lead product candidate, AI-700, would delay our receipt of product revenues and materially adversely affect our business, financial condition and results of operations.

We cannot be certain that we will obtain any regulatory approvals in other countries and the failure to obtain these approvals may materially adversely affect our business, financial condition and results of operations. In order to market our products outside of the United States, we and our collaborative partners, if any, must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. The approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks associated with obtaining FDA approval detailed above. Approval by the FDA does not ensure approval by the regulatory authorities of other countries. In addition, many countries outside the United States require a separate review process prior to marketing to determine whether their national health insurance scheme will pay for newly approved products, as well as the price which may be charged for a product.

Our products, if approved, may fail to achieve market acceptance.

There can be no assurance that any products we successfully develop, if approved for marketing, will achieve market acceptance or generate significant revenues. Each of our product candidates is intended to replace or alter existing therapies or procedures, and hospitals, physicians or patients may conclude that these products are less safe or effective or otherwise less attractive than these existing therapies or procedures. For example, our lead product candidate, AI-700, is a contrast agent for use in ultrasound imaging procedures which will compete with existing nuclear imaging and stress echocardiography. Hospitals, physicians or patients may prefer these existing procedures to AI-700 enhanced ultrasound imaging. If our products do not receive market acceptance for any reason, it would adversely affect our business, financial condition and results of operations.

Further, our competitors may develop new technologies or products that are more effective or less costly, or that seem more cost-effective, than our products. We can give no assurance that hospitals, physicians, patients or the medical community in general will accept and use any products that we may develop.

If we cannot raise additional capital on acceptable terms, we may be unable to complete planned clinical trials, obtain regulatory approvals or commercialize our product candidates.

We will require substantial future capital in order to continue to conduct the research and development, clinical and regulatory activities necessary to bring our product candidates to market and to establish commercial manufacturing, marketing and sales capabilities. Our future capital requirements will depend on many factors, including:

- the progress of pre-clinical development and laboratory testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the number of product candidates we pursue;
- the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims; and
- the establishment of selected strategic alliances and activities required for product commercialization.

We intend to seek additional funding through strategic collaborations and may seek funding through private or public sales of our securities or by licensing all or a portion of our technology. This funding may significantly dilute existing stockholders or may limit our rights to our technology.

We cannot assure you that we can obtain additional funding on reasonable terms, or at all. If we cannot obtain adequate funds, we may:

- terminate or delay clinical trials for one or more of our product candidates;
- delay our establishment of sales, marketing and/or manufacturing capabilities;
- curtail significant product development programs that are designed to identify new product candidates; and/or
- relinquish rights to our technologies or product candidates.

We believe that existing cash reserves will fund our planned activities for at least twelve months.

Claims by other companies that we infringe their proprietary technology may result in liability for damages or stop our development and commercialization efforts.

Competitors and other third parties may initiate patent litigation against us in the United States or in foreign countries based on existing patents or patents that may be granted in the future. Many of our competitors have obtained patents covering products and processes generally related to our products and processes, and they may assert these patents against us. Moreover, there can be no assurance that these competitors have not sought or will not seek additional patents that may cover aspects of our technology. As a result, there is a greater likelihood of a patent dispute than would be expected if our competitors were pursuing unrelated technologies.

While we conduct patent searches to determine whether the technologies used in our products infringe patents held by third parties, numerous patent applications are currently pending and may be filed in the future for technologies generally related to our technologies, including many patent applications that remain confidential after filing. Due to these factors and the inherent uncertainty in conducting patent searches, there can be no guarantee that we will not violate third-party patent rights that we have not yet identified.

We know of U.S. and foreign patents issued to third parties that relate to aspects of our product candidates. There may also be patent applications filed by these or other parties in the United States and various foreign jurisdictions that relate to some aspects of our product candidates, which, if issued, could subject us to infringement actions. In particular, we are aware of U.S. and foreign patents owned by third parties, including potential competitors, that arguably cover aspects of our AI-700 contrast agent. We and several of these parties have recently been actively engaged in opposing the grant of European patents with claims that arguably cover aspects of our AI-700 product. Parties may contest patents in Europe prior to contesting the counterpart patents in the United States because of procedural differences between European and U.S. patent laws as well as economic considerations. There is a significant possibility that one or more of these third parties will use litigation to assert their patents in the United States.

The owners or licensees of these and other patents may file one or more infringement actions against us. In addition, a competitor may claim misappropriation of a trade secret by an employee hired from that competitor. Any such infringement or misappropriation action could cause us to incur substantial costs defending the lawsuit and could distract our management from our business, even if the allegations of infringement or misappropriation are unwarranted. The defense of multiple claims could have a disproportionately greater impact. Furthermore, a party making this type of claim could secure a judgment that requires us to pay substantial damages. A judgment could also include an injunction or other court order that could prevent us from making, using, selling, offering for sale or importing our products or prevent our customers from using our products. If a court determined or if we independently discovered that any of our products or manufacturing processes violated third-party proprietary rights, there can be no assurance that we would be able to reengineer the product or processes to avoid those rights, or to obtain a license under those rights on commercially reasonable terms, if at all.

If we are unable to protect our intellectual propriety rights, our competitors may develop and market products with similar features that may reduce demand for our products, and we may be prevented from establishing collaborative relationships on favorable terms.

The following factors are important to our success:

- receiving patent protection for our product candidates;
- maintaining our trade secrets;
- not infringing on the proprietary rights of others; and
- preventing others from infringing our proprietary rights.

We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets.

We try to protect our proprietary position by filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. Because the patent position of pharmaceutical companies involves complex legal and factual questions, the issuance, scope and enforceability of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. Thus, any patents that we own or license from others may not provide any protection against competitors. Our pending patent applications, those we may file in the future, or those we may license from third parties, may not result in patents being issued. If issued, they may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, others may independently develop similar technologies or duplicate any technology that we have developed. The laws of many foreign countries do not protect our intellectual property rights to the same extent as do the laws of the United States.

We also rely on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. We try to protect this information by entering into confidentiality agreements with parties that have access to it, such as our corporate partners, collaborators, employees and consultants. Any of these parties may breach the agreements and disclose our confidential information or our competitors might learn of the information in some other way. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business and financial condition could be materially adversely affected.

We may become involved in lawsuits to protect or enforce our patents that would be expensive and time consuming.

In order to protect or enforce our patent rights, we may initiate patent litigation against third parties in the United States or in foreign countries. In addition, we may become subject to interference or opposition proceedings conducted in patent and trademark offices to determine the priority of inventions. The defense of intellectual property rights, including patent rights through lawsuits, interference or opposition proceedings, and other legal and administrative proceedings would be costly and divert our technical and management personnel from their normal responsibilities. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. For example, during the course of this kind of litigation, confidential information may be inadvertently disclosed in the form of documents or testimony in connection with discovery requests, depositions or trial testimony. This disclosure could materially adversely affect our business and financial results.

If third-party manufacturers of our products fail to devote sufficient time and resources to our concerns, or if their performance is substandard, our clinical trials and product introductions may be delayed and our costs may rise.

We have limited manufacturing facilities, and we have no experience in the commercial manufacturing of drugs and limited experience in designing drug manufacturing equipment. We have contracted with third party manufacturers to produce, in collaboration with us, our product candidates for clinical trials. We intend to rely, in part, on third-party contract manufacturers to supply, store and distribute our potential products for our clinical trials. We may continue to rely on third-parties to manufacture and distribute our potential products. Our reliance on these third-party manufacturers will expose us to the following risks, any of which could delay or prevent the completion of our clinical trials, the approval of our products by the FDA, or the commercialization of our products, result in higher costs, or deprive us of potential product revenues:

- Contract manufacturers often encounter difficulties in achieving volume production, quality control and quality assurance, as well as shortages of qualified personnel. Accordingly, a manufacturer might not be able to manufacture sufficient quantities of drugs to meet our clinical schedules or to commercialize our products.
- Contract manufacturers are obliged to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs. A failure of these contract manufacturers to establish and follow cGMPs and to document their adherence to such practices may lead to significant delays in the availability of material for clinical study and may delay or prevent filing or approval of marketing applications for our products.
- For each of our current product candidates we will initially rely on a single manufacturer. Changing these or future manufacturers may be difficult and the number of potential manufacturers is limited. Changing manufacturers may require re-validation of the manufacturing processes and procedures in accordance with FDA-mandated cGMPs. Such re-validation may be costly and time-consuming. It may be difficult or impossible for us to find replacement manufacturers on acceptable terms quickly, or at all.
- Our contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to produce, store and distribute our products successfully.

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the U.S. Drug Enforcement Agency, or the DEA, and corresponding state and foreign agencies to ensure strict compliance with cGMPs, other government regulations and corresponding foreign standards. While we are obligated to audit the performance of third party contractors, we do not have control over our third-party manufacturers' compliance with these regulations and standards. Failure by our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of product, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

In the event that we decide to manufacture all or a portion of our potential products for commercial use, we may encounter similar difficulties and challenges as well as the need to create cGMP compliant facilities.

We may not be able to manufacture our products in commercial quantities, which would prevent us from marketing our products.

To date our product candidates have been manufactured in small quantities for pre-clinical and clinical trials. If any of these product candidates are approved by the FDA or foreign regulatory authorities for commercial sale, we will need to manufacture them in larger quantities. We cannot assure you that we will be able to successfully increase the manufacturing capacity, whether on our own or in collaboration

with third party manufacturers, for any of our product candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require certain additional validation studies, which the FDA must review and approve. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply of that product candidate. Our product candidates require precise, high quality manufacturing. Our failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

Materials necessary to manufacture our products may not be available, which may delay our development and commercialization activities.

Only a few facilities manufacture some of the raw materials necessary to manufacture our products. For example, the manufacture of AI-850 will require bulk quantities of paclitaxel, a natural substance that is difficult to produce and is in limited supply. We currently have no supply agreements in place with any supply facility. If we need to purchase a raw material that is in limited supply for our clinical trials, or for commercial distribution if we obtain marketing approval of a product candidate, we cannot assure you that one or more suppliers would be able to sell us that raw material at the time we need it and on commercially reasonable terms. If we change suppliers for any of these materials or any of our suppliers experiences a shutdown or disruption in the facilities used to produce these materials, due to technical, regulatory or other problems, it could harm our ability to manufacture our products. Our inability to obtain required raw materials for any reason could substantially impair our development activities or the production, marketing and distribution of our products.

We have no experience selling, marketing or distributing our products and no internal capability to do so.

If we receive regulatory approval to commence commercial sales of any of our products, we will face competition with respect to commercial sales, marketing and distribution. These are areas in which we have no experience. To market any of our products directly, we must develop a direct marketing and sales force with technical expertise and supporting distribution capability. Alternatively, we may engage a pharmaceutical or other healthcare company with an existing distribution system and direct sales force to assist us. There can be no assurance that we will successfully establish sales and distribution capabilities either on our own or in collaboration with third parties or gain market acceptance for our products. To the extent we enter co-promotion or other licensing arrangements, any revenues we receive will depend on the efforts of third parties and there can be no assurance that our efforts will succeed.

We will establish collaborative relationships, and those relationships may expose us to a number of risks.

We will rely on a number of significant collaborative relationships with pharmaceutical or other healthcare companies for our manufacturing, research funding, clinical development and/or sales and marketing performance. Reliance on collaborative relationships poses a number of risks, including the following:

- we cannot effectively control whether our corporate partners will devote sufficient resources to our programs or product candidates;
- disputes may arise in the future with respect to the ownership of rights to technology developed with collaborators;
- disagreements with collaborators could delay or terminate the research and development, regulatory approval or commercialization of product candidates, or result in litigation or arbitration;

- corporate partners have considerable discretion in electing whether to pursue the development of any additional product candidates and may pursue technologies or products either on their own or in collaboration with our competitors; and
- collaborators with marketing rights may choose to devote fewer resources to the marketing of our product candidates than they do to product candidates of their own development.

For example, we established a joint venture with Elan Corporation, plc and affiliates in 2000. At the time, we anticipated that we would share the cost of pre-clinical and clinical trials for product candidates being developed by the joint venture with Elan. In 2002, for reasons beyond our control, Elan ceased funding the joint venture and the joint venture was terminated. In connection with the termination, we agreed to pay Elan a royalty if we commercialize the asthma product candidate that was being developed by the joint venture. Future development of product candidates will require that we provide all the funding for the cost of development and clinical trials or identify collaborators to share in the costs.

Given these risks, our current and future collaborative efforts may not be successful. Failure of these efforts could delay our product development or impair commercialization of our products, and have a material adverse effect on our business, financial condition and results of operations.

Competition in the pharmaceutical industry is intense, and if we fail to compete effectively our financial results will suffer.

We engage in a business characterized by extensive research efforts, rapid developments and intense competition. We cannot assure you that our products will compete successfully or that research and development by others will not render our products obsolete or uneconomical. Our failure to compete effectively would materially adversely affect our business, financial condition and results of operations. We expect that successful competition will depend, among other things, on product efficacy, safety, reliability, availability, timing and scope of regulatory approval and price. Specifically, we expect important factors will include the relative speed with which we can develop products, complete the clinical, development and laboratory testing and regulatory approval processes and supply commercial quantities of the product to the market.

We expect competition to increase as technological advances are made and commercial applications broaden. In commercializing our initial product candidates and any additional products we develop using our HDDS and PDDS technologies, we will face substantial competition from large pharmaceutical, biotechnology and other companies, universities and research institutions.

- AI-700, our ultrasound contrast agent and lead product candidate, if approved for marketing and sale, will compete with nuclear stress tests, the current standard of care in myocardial perfusion imaging. Nuclear contrast agents that are approved for use in myocardial perfusion imaging include products marketed by Amersham, Bristol-Myers Squibb and Tyco International. In addition, Amersham, Bristol-Myers Squibb and Imcor have developed ultrasound contrast agents that have been approved by the FDA for resting wall motion studies, and in the future they may seek to broaden their products to include stress echo and myocardial perfusion assessment. Moreover, we are aware that other companies, such as Bracco, are developing ultrasound contrast agents for wall imaging and for radiology applications, and that Point Biomedical is developing an ultrasound contrast agent specifically for myocardial perfusion imaging. In March 2004, Point announced that it had recently completed two pivotal Phase III trials for this contrast agent and plans to file an NDA with the FDA later this year. Finally, some cardiologists may find it satisfactory to use stress echo without contrast for the detection of coronary artery disease.
- AI-850, our reformulation of paclitaxel, if approved for marketing and sale, will also face intense competition from companies such as American Pharmaceutical Partners, NeoPharm and Sonus Pharmaceuticals, which are applying significant resources and expertise to developing reformulations of paclitaxel for intravenous delivery. Other companies, such as Cell Therapeutics, are developing new chemical entities that involve paclitaxel conjugated, or chemically bound, to another chemical.

- AI-128, our sustained release formulation of an asthma drug, if approved for marketing and sale, will also face intense competition. Companies such as Alkermes possess technology that may be suitable for sustained release pulmonary drug delivery and may have competitive programs that have not been publicly announced or may decide to begin such programs in the future. In addition, large pharmaceutical companies that market FDA-approved asthma drugs may be developing sustained release versions of their asthma drugs that would compete with our product candidates.

Relative to us, most of our competitors have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical trials and obtaining regulatory approvals, as well as in manufacturing and marketing pharmaceutical products. Many of our competitors may achieve product commercialization or patent protection earlier than we will. Furthermore, we believe that some of our competitors have used, and may continue to use, litigation to gain a competitive advantage. Finally, our competitors may use different technologies or approaches to the development of products similar to the products we are seeking to develop.

If we are unable to retain key personnel and hire additional qualified scientific, sales and marketing, and other personnel, we may not be able to successfully achieve our goals.

We depend on the principal members of our scientific and management staff, including Sherri C. Oberg, our president and chief executive officer, John F. Thero, our senior vice president and chief financial officer, Howard Bernstein, our senior vice president of research and development, Charles P. Cox, our senior vice president of corporate development and marketing, and Michael R. Slater, our senior vice president of operations. The loss of any of these individuals' services might significantly delay or prevent the achievement of research, development or business objectives and could materially adversely affect our business, financial condition and results of operations. We do not maintain key person life insurance on any of these individuals.

Ms. Oberg and Dr. Bernstein are critical to the development of our technologies and business. Dr. Cox, who joined us in August 2003, Mr. Thero, who joined us in February 2003, and Mr. Slater, who joined us in October 2001, are key additions to our management team and are also critical to directing and managing our growth and development in the future. We are not aware of any present intention of any of these individuals to leave our company. We have no employment contracts with any of our employees.

Our success depends, in large part, on our ability to attract and retain qualified scientific and management personnel such as these individuals. We face intense competition for such personnel and consultants. We cannot assure you that we will attract and retain qualified management and scientific personnel in the future.

Further, we expect that our potential expansion into areas and activities requiring additional expertise, such as further clinical trials, governmental approvals, commercial manufacturing and marketing, will place additional requirements on our management, operational and financial resources. We expect these demands will require an increase in management and scientific personnel and the development of additional expertise by existing management personnel. The failure to attract and retain such personnel or to develop such expertise could materially adversely affect prospects for our success.

We expect to develop international operations that will expose us to additional business risks.

In the future, we expect to develop operations outside the United States in order to market and distribute our products. We cannot be sure that our international efforts will be successful. Any expansion into international markets will require additional resources and management attention and will subject us to new business risks. These risks could lower the prices at which we can sell our products or otherwise

have an adverse effect on our operating results. Among the risks we believe are most likely to affect any international operations are:

- different regulatory requirements for approval of our product candidates;
- dependence on local distributors;
- longer payment cycles and problems in collecting accounts receivable;
- adverse changes in trade and tax regulations;
- the absence or significant lack of legal protection for intellectual property rights;
- political and economic instability; and
- currency risks.

Risks Relating to Our Industry

Even if we obtain marketing approval, our products will be subject to ongoing regulatory review.

If regulatory approval of a product is granted, such approval may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for costly, post-marketing follow-up studies. As to products for which marketing approval is obtained, the manufacturer of the product and the manufacturing facilities will be subject to continual review and periodic inspections by the FDA and other regulatory authorities. In addition, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping related to the product will remain subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the product, manufacturer or facility may result in restrictions on the product or the manufacturer, including withdrawal of the product from the market. We may be slow to adapt, or we may never adapt, to changes in existing requirements or adoption of new requirements or policies.

If we fail to comply with applicable regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Market acceptance of our products will be limited if users of our products are unable to obtain adequate reimbursement from third-party payors.

Government health administration authorities, private health insurers and other organizations generally provide reimbursement for products like our product candidates, and our commercial success will depend in part on these third-party payors agreeing to reimburse patients for the costs of our products. Even if we succeed in bringing any of our proposed products to market, we cannot assure you that third-party payors will consider our products cost-effective or provide reimbursement in whole or in part for their use.

Significant uncertainty exists as to the reimbursement status of newly approved health care products. Each of our product candidates is intended to replace or alter existing therapies or procedures. These third-party payors may conclude that our products are less safe, effective or cost-effective than these existing therapies or procedures. Therefore, third-party payors may not approve our products for reimbursement.

If third-party payors do not approve our products for reimbursement or fail to reimburse them adequately, sales will suffer as some physicians or their patients will opt for a competing product that is approved for reimbursement or is adequately reimbursed. Even if third-party payors make reimbursement available, these payors' reimbursement policies may adversely affect the ability of us and our potential collaborators to sell our products on a profitable basis.

Moreover, the trend toward managed healthcare in the United States, the growth of organizations such as health maintenance organizations, and legislative proposals to reform healthcare and government insurance programs could significantly influence the purchase of healthcare services and products, resulting

in lower prices and reduced demand for our products which could adversely affect our business, financial condition and results of operations.

In addition, legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us before or after the FDA or other regulatory agencies approve any of our proposed products for marketing. While we cannot predict the likelihood of any of these legislative or regulatory proposals, if any government or regulatory agencies adopt these proposals they could materially adversely affect our business, financial condition and results of operations.

We may be required to defend lawsuits or pay damages in connection with the alleged or actual harm caused by our products or product candidates.

We face an inherent business risk of exposure to product liability claims in the event that the use of our products is alleged to have resulted in harm to others. This risk exists in clinical trials as well as in commercial distribution. In addition, the pharmaceutical and biotechnology industries in general have been subject to significant medical malpractice litigation. We may incur significant liability if product liability or malpractice lawsuits against us are successful. Furthermore, product liability claims, regardless or their merits, could be costly and divert our management's attention from other business concerns, or adversely affect our reputation and the demand for our products. Although we maintain product liability insurance, we cannot be certain that this coverage will be adequate or that it will continue to be available to us on acceptable terms.

Rapid technological change could make our products obsolete.

Pharmaceutical technologies have undergone rapid and significant change. We expect that pharmaceutical technologies will continue to develop rapidly. Our future will depend in large part on our ability to maintain a competitive position with respect to these technologies. Any compounds, products or processes that we develop may become obsolete before we recover any expenses incurred in connection with their development. Rapid technological change could make our products obsolete, which could materially adversely affect our business, financial condition and results of operations.

Our products involve the use of hazardous materials, and as a result we are exposed to potential liability claims and to costs associated with complying with laws regulating hazardous waste.

Our research and development activities involve the use of hazardous materials, including chemicals and biological materials. We believe that our procedures for handling hazardous materials comply with federal and state regulations. However, there can be no assurance that accidental injury or contamination from these materials will not occur. In the event of an accident, we could be held liable for any damages, which could exceed our available financial resources. This liability could materially adversely affect our business, financial condition and results of operations.

We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products, and we spent approximately $32,000 in 2003 to dispose of these hazardous materials and waste products. We may be required to incur significant costs to comply with environmental laws and regulations in the future that could materially adversely affect our business, financial condition and results of operations.

Risks Related to Our Common Stock

We expect that our stock price will fluctuate significantly.

We only recently completed our initial public offering. Prior to this offering, you could not buy or sell our common stock publicly. An active public market for our common stock may not continue to develop or be sustained. The stock market, particularly in recent years, has experienced significant volatility particularly with respect to pharmaceutical and biotechnology stocks. The volatility of pharmaceutical and

biotechnology stocks often does not relate to the operating performance of the companies represented by the stock. Factors that could cause this volatility in the market price of our common stock include:

- announcements of the introduction of new products by us or our competitors;
- market conditions in the pharmaceutical and biotechnology sectors;
- rumors relating to us or our competitors;
- litigation or public concern about the safety of our potential products;
- our quarterly operating results;
- deviations in our operating results from the estimates of securities analysts; and
- FDA or international regulatory actions.

We may be the subject of securities class action litigation due to future stock price volatility.

In the past, when the market price of a stock has been volatile, holders of that stock have often instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Future sales of common stock by our existing stockholders may cause our stock price to fall.

The market price of our common stock could decline as a result of sales by our existing stockholders of shares of common stock in the market, or the perception that these sales could occur. These sales might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate. In connection with our recently completed initial public offering, our executive officers and directors and substantially all of our pre-initial public offering stockholders and optionholders executed lock-up agreements that prohibit them from offering, selling, contracting to sell, granting an option to purchase, making a short sale or otherwise disposing of any shares of our common stock or any option to purchase shares of our common stock or any securities exchangeable for or convertible into shares of common stock for the 180 day period from the date of our initial public offering through April 4, 2004 without the prior written consent of SG Cowen Securities Corporation. SG Cowen has no pre-established conditions to waiving the terms of the lock-up agreements, and any decision by it to waive those conditions would depend on a number of factors, including market conditions, the performance of the common stock in the market and our financial condition at that time.

Our directors and management will exercise significant control over our company.

Our directors and executive officers and their affiliates collectively control approximately 42.0% of our outstanding common stock, excluding unexercised options and warrants. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

Provisions of Delaware law or our charter documents could delay or prevent an acquisition of us, even if the acquisition would be beneficial to our stockholders, and could make it more difficult for you to change management.

Provisions of Delaware law or our charter or by-laws could hamper a third party's acquisition of us, or discourage a third party from attempting to acquire control of us. Stockholders who wish to participate in these transactions may not have the opportunity to do so. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock. Further, these provisions make it more difficult for stockholders to change the composition of our board of directors in any one year.

These provisions include:

- a provision allowing us to issue preferred stock with rights senior to those of the common stock without any further vote or action by the holders of the common stock;
- the existence of a staggered board of directors in which there are three classes of directors serving staggered three-year terms, thus expanding the time required to change the composition of a majority of directors and potentially discouraging someone from making an acquisition proposal for us;
- the by-laws' requirement that stockholders provide advance notice when nominating our directors;
- the inability of stockholders to convene a stockholders' meeting without the chairperson of the board, the chief executive officer, the president or a majority of the board of directors first calling the meeting; and
- the application of Delaware law prohibiting us from entering into a business combination with the beneficial owner of 15% or more of our outstanding voting stock for a period of three years after the 15% or greater owner first reached that level of stock ownership, unless we meet specified criteria.

It is also likely that events arising out of the conviction of Arthur Andersen would adversely affect its ability to satisfy any claims we may have arising from its provision of auditing and other services to us. Such services were provided to us by Arthur Andersen before June 7, 2002.

We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our businesses. In addition, the terms of any future debt or credit facility may preclude us from paying these dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

We have not used derivative financial instruments for speculation or trading purposes. However, we are exposed to market risk related to changes in interest rates. Our current policy is to maintain an investment portfolio consisting mainly of U.S. money market and government-grade securities, directly or through managed funds, with maturities of one year or less. Our cash is deposited in and invested through highly rated financial institutions in North America. Our short-term investments are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 10% from levels at December 31, 2003, we estimate that the fair value of our investment portfolio would decline by an immaterial amount. We currently have the ability to hold our fixed income investments until maturity, and therefore we do not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Effects of Inflation

Our assets are primarily monetary, consisting of cash, cash equivalents and short-term investments. Because of their liquidity, these assets are not directly affected by inflation. We also believe that we have intangible assets in the value of our technology. In accordance with generally accepted accounting principles, we have not capitalized the value of this intellectual property on our consolidated balance sheet. Due to the nature of this intellectual property, we believe that these intangible assets are not affected by inflation. Because we intend to retain and continue to use our equipment, furniture and fixtures and leasehold improvements, we believe that the incremental inflation related to replacement costs of such items will not materially affect our operations. However, the rate of inflation affects our expenses, such as

those for employee compensation and contract services, which could increase our level of expenses and the rate at which we use our resources.

Item 8. ***Financial Statements***

Our Financial Statements, together with the independent auditors' report, appear at pages F-2 through F-28, respectively, of this Form 10-K.

Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

On June 7, 2002, upon the recommendation of our audit committee and authorization by our board of directors, we dismissed Arthur Andersen LLP as our independent accountants and engaged Deloitte & Touche LLP as our independent accountants.

During the year ended December 31, 2000, and the interim period from December 31, 2000 to June 7, 2002, Arthur Andersen did not have any disagreement with us on any matter of accounting principles or practices, financial statement disclosure or auditing scope or procedure, which disagreement, if not resolved to the satisfaction of Arthur Andersen, would have caused it to make reference to the subject matter of the disagreement in connection with its report on our financial statements. The report of Arthur Andersen on our consolidated financial statements for our fiscal year ended December 31, 2000 did not contain an adverse opinion or disclaimer of opinion, and was not qualified or modified as to uncertainty, audit scope or accounting principles. We did not consult with Deloitte & Touche LLP on any financial or accounting reporting matters in the period before its appointment.

Item 9A. ***Controls and Procedures***

Evaluation of Disclosure Controls and Procedures

As of December 31, 2003 (the "Evaluation Date"), the Company's management, with the participation of the Company's Chief Executive Officer and the Company's Senior Vice President and Chief Financial Officer, evaluated the effectiveness of the Company's disclosure controls and procedures pursuant to Rule 13a-15(b) promulgated under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Based upon that evaluation, the Company's Chief Executive Officer and the Company's Senior Vice President and Chief Financial Officer concluded that, as of the Evaluation Date, the Company's disclosure controls and procedures were effective in ensuring that material information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, including ensuring that such material information is accumulated and communicated to the Company's management, including the Company's Chief Executive Officer and the Company's Senior Vice President and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

Internal Control Over Financial Reporting

During the period covered by this report, there have been no changes in the Company's internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

PART III

Item 10. ***Directors and Executive Officers of the Registrant***

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2003.

Code of Ethics

We have adopted a "code of ethics" as defined by regulations promulgated under the Securities Act of 1933, as amended, and the Exchange Act of 1934, as amended, and a "code of conduct" as defined by qualitative listing requirements promulgated by the Nasdaq National Market that apply to all of our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We collectively refer to these codes as our Code of Business Conduct and Ethics, a current copy of which is attached as an exhibit to this Annual Report on Form 10-K. A current copy of our Code of Business Conduct and Ethics may also be obtained by any person, without charge, upon request directed to our Investor Relations department at: Acusphere, Inc., Attention: Investor Relations, 500 Arsenal Street, Watertown, MA 02472.

We intend to disclose amendments to or waivers (including implicit waivers) of any provision of the Code of Business Conduct and Ethics that apply to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, in compliance with applicable rules and regulations.

Item 11. ***Executive Compensation***

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2003.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2003.

Item 13. ***Certain Relationships and Related Transactions***

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2003.

Item 14. ***Principal Accountant Fees and Services***

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2003.

PART IV

Item 15. ***Exhibits, Financial Statement Schedules, and Reports on Form 8-K***

(a)1. Consolidated Financial Statements.

For a list of the financial information included herein, see Index on Page F-1.

2. Financial Statement Schedules.

Unaudited Quarterly Results of Operations, as previously reported for each of the fiscal quarters in the years ended December 31, 2002 and 2003, except for the unaudited results of operations for the fiscal quarter ended December 31, 2003 which is reported in this schedule and had not been previously reported. Except for the schedule of Unaudited Quarterly Results of Operations, no financial statement schedules

have been submitted because they are not required, not applicable, or because the information required is included in the financial statements or the notes thereto.

3. Exhibit Index.

Exhibit Number	Description
3.01	Amended and Restated Certificate of Incorporation of registrant (incorporated herein by reference to Exhibit 3.02 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
3.02	Amended and Restated By-laws of registrant (incorporated herein by reference to Exhibit 3.04 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
4.01	Specimen Certificate for shares of common stock of registrant (incorporated herein by reference to Exhibit 4.01 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.01†	1994 Stock Plan, as amended (incorporated herein by reference to Exhibit 10.01 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.02†	2003 Stock Plan (incorporated herein by reference to Exhibit 10.02 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.03†	2003 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.03 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.03†	Stock Repurchase and Registration Agreement by and among the registrant, Harry R. Allcock, Sherri C. Oberg, Robert S. Langer, Richard Kronenthal and Walter Levison, dated as of April 30, 1996 (incorporated herein by reference to Exhibit 10.05 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.04†	Letter Agreement by and among the registrant, Sherri C. Oberg and Robert S. Langer, dated as of April 30, 1996 (incorporated herein by reference to Exhibit 10.06 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.05	Tenth Amended and Restated Investors' Rights Agreement by and among registrant, Sherri C. Oberg and the Investors named therein, dated as of April 11, 2003, as amended (incorporated herein by reference to Exhibit 10.07 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.06	Lease Agreement by and between the registrant and Forest City 38 Sidney Street, Inc., dated as of April 18, 1995, as amended (incorporated herein by reference to Exhibit 10.08 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.07	Warrant Agreement by and between the registrant and Comdisco, Inc., dated as of June 6, 1997 (incorporated herein by reference to Exhibit 10.09 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.08	Warrant Agreement by and between the registrant and Comdisco, Inc., dated as of February 26, 1998 (incorporated herein by reference to Exhibit 10.10 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.09	Warrant Agreement by and between the registrant and Comdisco, Inc., dated as of August 19, 1998 (incorporated herein by reference to Exhibit 10.12 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.10	Warrant Agreement by and between the registrant and Gregory Stento, dated as of August 19, 1998(incorporated herein by reference to Exhibit 10.13 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.11	Warrant Agreement by and between the registrant and Gregory Stento, dated as of August 19, 1998 (incorporated herein by reference to Exhibit 10.14 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.12	Warrant Agreement by and between the registrant and Comdisco, Inc., dated as of October 16, 1998 (incorporated herein by reference to Exhibit 10.15 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.13	Warrant Agreement by and between the registrant and Comdisco, Inc., dated as of October 19, 1998 (incorporated herein by reference to Exhibit 10.16 to the registrant's Registration Statement on Form S-1, File No. 333-106725)

Exhibit Number	Description
10.14	Warrant Agreement by and between the registrant and Comdisco, Inc., dated as of January 5, 2000 (incorporated herein by reference to Exhibit 10.17 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.15	Master Lease Agreement by and among the registrant, Acusphere Securities Corporation and Transamerica Business Credit Corporation, dated as of February 21, 2001 (incorporated herein by reference to Exhibit 10.18 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.16	Warrant Agreement by and between the registrant and TBCC Funding Trust I, dated of February 21, 2001 (incorporated herein by reference to Exhibit 10.19 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.17	Lease Agreement, by and between registrant and ARE-500 Arsenal Street, LLC, dated as of March 30, 2001 (incorporated herein by reference to Exhibit 10.20 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.18	Warrant Agreement by and between the registrant and Alexandria Real Estate Equities, L.P., dated of March 30, 2001 (incorporated herein by reference to Exhibit 10.21 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.19	CTM Agreement by and between the registrant and Hollister-Stier Laboratories LLC, dated as of September 7, 2001 (incorporated herein by reference to Exhibit 10.22 to the registrant's Registration Statement on Form S-1, File No. 333-106725) (confidential treatment previously granted)
10.20	Development and Supply Agreement by and between the registrant and Hollister-Stier Laboratories LLC dated as of November 30, 2001 (incorporated herein by reference to Exhibit 10.23 to the registrant's Registration Statement on Form S-1, File No. 333-106725) (confidential treatment previously granted)
10.21	Warrant Agreement by and between the registrant and GATX Ventures, Inc., dated as of September 27, 2001 (incorporated herein by reference to Exhibit 10.25 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.22	Warrant Agreement by and between the registrant and Venture Lending & Leasing III, LLC, dated as of September 27, 2001 (incorporated herein by reference to Exhibit 10.26 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.23	Termination Agreement by and among the registrant, Acusphere Newco, Ltd., Elan Corporation, plc, Elan Pharma International Limited and Elan International Services, Ltd. dated as of September 26, 2003 (incorporated herein by reference to Exhibit 10.27 to the registrant's Registration Statement on Form S-1, File No. 333-106725) (confidential treatment previously granted)
10.24	Form of Indemnification Agreement by and between the registrant and each of its directors (incorporated herein by reference to Exhibit 10.28 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.25	Form of Warrant issued by the registrant dated as of April 11, 2003 and June 27, 2003 to each of the investors listed on the schedule of warrantholders attached thereto (incorporated herein by reference to Exhibit 10.29 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
10.26†	Form of Indemnification Agreement by and between the registrant and certain of its employees (incorporated herein by reference to Exhibit 10.30 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
14.01*	Code of Ethics
21.01	List of Subsidiaries (incorporated herein by reference to Exhibit 21.01 to the registrant's Registration Statement on Form S-1, File No. 333-106725)
23.01*	Consent of Deloitte & Touche LLP relating to the consolidated financial statements of Acusphere, Inc.
24.01	Power of Attorney (included in signature page)

Exhibit Number	Description
31.1*	Certification Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Exchange Act, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Exchange Act, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1*	Certification Pursuant to 18 u.s.c. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

* Filed herewith.

† Indicates a management contract or any compensatory plan, contract or arrangement.

The other exhibits listed have previously been filed with the Securities and Exchange Commission and are incorporated herein by reference, as indicated.

(b) Reports on Form 8-K.

We furnished a current report on Form 8-K on November 12, 2003 to furnish to the SEC under Item 12 of Form 8-K a copy of our quarterly earnings release for the fiscal quarter ended September 30, 2003.

(c) Exhibits.

We hereby file as part of this Form 10-K the exhibits listed in Item 15(a)(3) above. Exhibits which are incorporated herein by reference can be inspected and copied at the public reference facilities maintained by the Securities and Exchange Commission, 450 Fifth Street, N.W., Washington, D.C., and at the Commission's regional offices at Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, IL 60611-2511, and at 233 Broadway, New York, NY 10279. Copies of such material can also be obtained from the Public Reference Section of the Commission, 450 Fifth Street, N.W., Washington, D.C. 29549, at prescribed rates.

(d) Financial Statement Schedule.

Unaudited Quarterly Results of Operations, as previously reported for each of the fiscal quarters in the years ended December 31, 2002 and 2003, except for the unaudited results of operations for the fiscal quarter ended December 31, 2003 which is reported in this schedule and had not been previously reported. Except for the schedule of Unaudited Quarterly Results of Operations, no financial statement schedules have been submitted because they are not required, not applicable, or because the information required is included in the financial statements or the notes thereto.

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.

ACUSPHERE, INC.

By: /s/ SHERRI C. OBERG
Sherri C. Oberg
President and Chief Executive Officer

Date: March 17, 2004

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Acusphere, Inc., hereby severally constitute and appoint Sherri C. Oberg and John F. Thero, and each of them singly, our true and lawful attorneys, with full power to them and each of them singly, to sign for us in our names in the capacities indicated below, all amendments to this report, and generally to do all things in our names and on our behalf in such capacities to enable Acusphere, Inc. to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all requirements of the Securities and Exchange Commission.

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/ SHERRI C. OBERG Sherri C. Oberg	President and Chief Executive Officer and Director (Principal Executive Officer)	March 17, 2004
/s/ JOHN F. THERO John F. Thero	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 17, 2004
/s/ TERRANCE MCGUIRE Terrance McGuire	Director	March 17, 2004
/s/ DEREK LEMKE-VON AMMON Derek Lemke-von Ammon	Director	March 17, 2004
/s/ KATE MITCHELL Kate Mitchell	Director	March 17, 2004
/s/ FRANK BALDINO Frank Baldino	Director	March 17, 2004
/s/ MARTYN GREENACRE Martyn Greenacre	Director	March 17, 2004

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

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INDEPENDENT AUDITORS' REPORT

To the Board of Directors and Shareholders of
Acusphere, Inc.
Watertown, Massachusetts

We have audited the accompanying consolidated balance sheets of Acusphere, Inc. and subsidiaries (the "Company") (a development stage company) as of December 31, 2002 and 2003, and the related consolidated statements of operations, redeemable convertible preferred stock, stockholders' (deficit) equity, and comprehensive loss, and cash flows for each of the three years in the period ended December 31, 2003 and for the period from July 12, 1993 (date of inception) through December 31, 2003. 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. The Company's financial statements for the period July 12, 1993 (date of inception) through December 31, 2000 were audited by other auditors who have ceased operations. The financial statements for the period July 12, 1993 (date of inception) through December 31, 2000 reflect total net losses of $53,113,128, of the related totals. The other auditors' report has been furnished to us, and our opinion, insofar as it relates to the amounts included for such prior period, is based solely on the report of such other auditors.

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

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2002 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended, December 31, 2003 and for the period from July 12, 1993 (date of inception) through December 31, 2003, in conformity with accounting principles generally accepted in the United States of America.

As discussed above, the consolidated financial statements of Acusphere, Inc. for the period from inception (July 12, 1993) to December 31, 2000 were audited by other auditors who have ceased operations. As described in Note 2, these financial statements have been adjusted to reflect a one-for-six reverse stock split that was effected on September 12, 2003. We audited the adjustments described in Note 2 that were applied to revise these financial statements. Our audit procedures included (1) comparing the previously reported shares issued and outstanding per the Company's accounting analysis to the previously issued financial statements, and (2) recalculating the reduction in shares to give effect to the reverse stock split and testing the mathematical accuracy of the underlying analysis. In our opinion, such adjustments and disclosures are appropriate and such adjustments have been properly applied. However, we were not engaged to audit, review or apply any procedures to the consolidated financial statements from inception (July 12, 1993) to December 31, 2000 of the Company other than with respect to such adjustments and, accordingly, we do not express an opinion or any other form of assurance on these consolidated financial statements taken as a whole.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts
March 15, 2004

This is a copy of a report previously issued by Arthur Andersen LLP. This report has not been reissued by Arthur Andersen LLP nor has Arthur Andersen LLP provided a consent to the inclusion of its report in these financial statements. The financial statements as of December 31, 1999 and 2000 and for each of the years in the three-year period ended December 31, 2000 are not presented herein.

REPORT OF INDEPENDENT PUBLIC ACCOUNTANTS

To the Stockholders and Board of Directors of
Acusphere, Inc. and Subsidiary:

We have audited the accompanying consolidated balance sheets of Acusphere, Inc. (a Delaware corporation in the development stage) and subsidiary (the Company) as of December 31, 1999 and 2000, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' deficit and cash flows for each of the years in the three-year period ended December 31, 2000 and for the period from inception (July 12, 1993) to December 31, 2000. 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 the Company as of December 31, 1999 and 2000, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2000 and for the period from inception (July 12, 1993) to December 31, 2000, in conformity with accounting principles generally accepted in the United States.

/s/ ARTHUR ANDERSEN LLP

Boston, Massachusetts
February 12, 2001

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)
CONSOLIDATED BALANCE SHEETS

	As of December 31, 2002	As of December 31, 2003
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 7,796,238	$ 54,562,378
Short-term investments	195,698	—
Other current assets	428,837	712,673
Total current assets	8,420,773	55,275,051
PROPERTY AND EQUIPMENT, at cost:		
Equipment and furniture	8,887,930	9,837,350
Leasehold improvements	98,195	122,505
Total property and equipment	8,986,125	9,959,855
Less accumulated depreciation and amortization	6,202,033	7,935,450
Property and equipment, net	2,784,092	2,024,405
OTHER ASSETS	2,162,196	1,624,797
TOTAL	$ 13,367,061	$ 58,924,253
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' (DEFICIT) EQUITY		
CURRENT LIABILITIES:		
Current portion of long-term obligations	$ 3,564,655	$ 884,799
Accounts payable	737,715	1,519,981
Accrued expenses	1,219,744	1,939,012
Total current liabilities	5,522,114	4,343,792
LONG-TERM OBLIGATIONS, net of current portion	1,725,588	205,418
COMMITMENTS (Notes 9 and 10)		
REDEEMABLE CONVERTIBLE PREFERRED STOCK, at carrying value; including accrued dividends; authorized, 32,106,077 and 5,000,000 shares as of December 31, 2002 and 2003, respectively; issued and outstanding, 31,145,083 and no shares as of December 31, 2002 and 2003, respectively	91,467,075	—
STOCKHOLDERS' (DEFICIT) EQUITY:		
Common stock, $0.01 par value; authorized, 11,741,127 and 98,500,000 shares as of December 31, 2002 and 2003, respectively; issued, 1,218,876 and 14,294,533 shares as of December 31, 2002 and 2003, respectively; outstanding, 1,212,849 and 14,294,533 shares as of December 31, 2002 and 2003, respectively	12,189	142,945
Additional paid-in capital	34,029,519	201,422,784
Less treasury stock, 6,027 shares, at cost	(361)	—
Accumulated other comprehensive income	288	—
Deferred stock-based compensation	(1,793,404)	(1,723,229)
Deficit accumulated during the development stage	(117,595,947)	(145,467,457)
Total stockholders' (deficit) equity	(85,347,716)	54,375,043
TOTAL	$ 13,367,061	$ 58,924,253

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,			Period from Inception (July 12, 1993) to December 31,
	2001	2002	2003	2003
OPERATING EXPENSES:				
Research and development(1)	$ 11,535,574	$ 13,545,084	$ 14,228,611	$ 72,553,098
General and administrative(1)	3,893,553	3,905,465	4,172,726	20,124,922
Stock-based compensation	1,075,606	2,195,202	1,307,052	4,667,585
Total operating expenses	16,504,733	19,645,751	19,708,389	97,345,605
Equity in loss of joint venture	(1,965,840)	(1,183,417)	—	(15,164,257)
Interest income	943,430	223,550	199,883	3,973,938
Other income(expense)	—	9,114	22,701	31,815
Interest expense	(750,049)	(1,299,746)	(2,437,632)	(6,705,898)
NET LOSS	(18,277,192)	(21,896,250)	(21,923,437)	(115,210,007)
Accretion of dividends and offering costs on preferred stock	(6,248,616)	(6,665,478)	(5,948,073)	(30,257,450)
NET LOSS AVAILABLE TO COMMON STOCKHOLDERS	$(24,525,808)	$(28,561,728)	$(27,871,510)	$(145,467,457)
NET LOSS AVAILABLE TO COMMON STOCKHOLDERS PER SHARE — Basic and diluted	$ (50.81)	$ (35.39)	$ (6.66)	
WEIGHTED-AVERAGE SHARES OUTSTANDING — Basic and diluted	482,713	807,119	4,187,672	
(1) Excludes stock-based compensation as follows:				
Research and development	$ 417,413	$ 915,085	$ 589,642	$ 1,994,143
General and administrative	658,193	1,280,117	717,410	2,673,442
	$ 1,075,606	$ 2,195,202	$ 1,307,052	$ 4,667,585

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional Paid-in Capital	Treasury Stock		Accumulated Other Comprehensive Income	Deferred Stock-Based Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' (Deficit) Equity	Comprehensive Loss
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value		Number of Shares	Cost					
INCEPTION OF COMPANY, JULY 12, 1993												
Sale of common stock	—	$ —	416,664	$ 4,167	$ 20,833	—	$ —	$ —	$ —	$ (19,819)	$ 5,181	
Sale of Series A Redeemable Convertible Preferred Stock, net of stock issuance costs of $26,813	775,000	748,187	—	—	—	—	—	—	—	—	—	
Accretion of offering costs	—	1,957	—	—	—	—	—	—	—	(1,957)	(1,957)	
Net loss	—	—	—	—	—	—	—	—	—	(561,812)	(561,812)	$ (561,812)
BALANCE, DECEMBER 31, 1994	775,000	750,144	416,664	4,167	20,833	—	—	—	—	(583,588)	(558,588)	
Sale of common stock	—	—	5,585	56	3,295	—	—	—	—	—	3,351	
Sale of Series B Redeemable Convertible Preferred Stock, net of issuance costs of $45,024	2,265,625	3,579,976	—	—	—	—	—	—	—	—	—	
Issuance of common stock for services performed	—	—	32,435	324	20,829	—	—	—	—	—	21,153	
Issuance of preferred stock for services performed	41,169	41,169	—	—	—	—	—	—	—	—	—	
Purchase of treasury stock	—	—	—	—	—	6,027	(361)	—	—	—	(361)	
Accretion of offering costs	—	5,055	—	—	—	—	—	—	—	(5,055)	(5,055)	
Net loss	—	—	—	—	—	—	—	—	—	(1,970,102)	(1,970,102)	$ (1,970,102)
BALANCE, DECEMBER 31, 1995	3,081,794	4,376,344	454,684	4,547	44,957	6,027	(361)	—	—	(2,558,745)	(2,509,602)	
Exercise of stock options	—	—	1,736	17	1,094	—	—	—	—	—	1,111	
Issuance of common stock for services performed	—	—	6,322	63	7,102	—	—	—	—	—	7,165	
Sale of Series C Redeemable Convertible Preferred Stock, net of issuance costs of $44,915	3,913,551	8,330,084	—	—	—	—	—	—	—	—	—	
Purchase and retirement of common stock	—	—	(47,860)	(479)	(520)	—	—	—	—	—	(999)	

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS — (Continued)
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional Paid-in Capital	Treasury Stock		Accumulated Other Comprehensive Income	Deferred Stock-Based Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' (Deficit) Equity	Comprehensive Loss
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value		Number of Shares	Cost					
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(17,499)	—	—	(17,499)	$ (17,499)
Accretion of dividends and offering costs on preferred stock	—	720,015	—	—	—	—	—	—	—	(720,015)	(720,015)	
Net loss	—	—	—	—	—	—	—	—	—	(2,633,519)	(2,633,519)	(2,633,519)
Comprehensive net loss												$ (2,651,018)
BALANCE, DECEMBER 31, 1996	6,995,345	13,426,443	414,882	4,148	52,633	6,027	(361)	(17,499)	—	(5,912,279)	(5,873,358)	
Exercise of stock options	—	—	352	4	207	—	—	—	—	—	211	
Sale of Series D Redeemable Convertible Preferred Stock, net of issuance costs of $39,895	3,405,624	10,176,977	—	—	—	—	—	—	—	—	—	
Unrealized gain on short-term investments	—	—	—	—	—	—	—	19,367	—	—	19,367	$ 19,367
Accretion of dividends and offering costs on preferred stock	—	1,435,260	—	—	—	—	—	—	—	(1,435,260)	(1,435,260)	
Net loss	—	—	—	—	—	—	—	—	—	(4,942,576)	(4,942,576)	(4,942,576)
Comprehensive net loss												$ (4,923,209)
BALANCE, DECEMBER 31, 1997	10,400,969	25,038,680	415,234	4,152	52,840	6,027	(361)	1,868	—	(12,290,115)	(12,231,616)	
Exercise of stock options	—	—	6,570	66	4,755	—	—	—	—	—	4,821	
Sale of Series E Redeemable Convertible Preferred Stock, net of issuance costs of $13,140	757,577	2,486,864	—	—	—	—	—	—	—	—	—	
Deferred stock-based compensation related to issuance of common stock for services performed	—	—	8,334	83	16,417	—	—	—	(16,500)	—	—	
Issuance of Series D and E Redeemable Convertible Preferred Stock warrants in connection with debt offering	—	—	—	—	311,000	—	—	—	—	—	311,000	

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS — (Continued)
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional	Treasury Stock		Accumulated Other	Deferred	Deficit Accumulated During the	Total	
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value	Paid-in Capital	Number of Shares	Cost	Comprehensive Income	Stock-Based Compensation	Development Stage	Stockholders' (Deficit) Equity	Comprehensive Loss
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(694)	—	—	(694)	$ (694)
Accretion of dividends and offering costs on preferred stock	—	2,410,878	—	—	—	—	—	—	—	(2,410,878)	(2,410,878)	
Net loss	—	—	—	—	—	—	—	—	—	(9,415,091)	(9,415,091)	(9,415,091)
Comprehensive net loss												$ (9,415,785)
BALANCE, DECEMBER 31, 1998	11,158,546	$ 29,936,422	430,138	$ 4,301	$ 385,012	6,027	$(361)	$ 1,174	$ (16,500)	$ (24,116,084)	$(23,742,458)	
Exercise of stock options	—	—	3,500	35	2,265	—	—	—	—	—	2,300	
Deferred stock-based compensation related to issuance of common stock options to nonemployees for services performed	—	—	—	—	9,562	—	—	—	(9,562)	—	—	
Amortization of deferred stock-based compensation	—	—	—	—	—	—	—	—	4,620	—	4,620	
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(1,174)	—	—	(1,174)	$ (1,174)
Accretion of dividends and offering costs on preferred stock	—	2,603,723	—	—	—	—	—	—	—	(2,603,723)	(2,603,723)	
Net loss	—	—	—	—	—	—	—	—	—	(9,141,450)	(9,141,450)	(9,141,450)
Comprehensive net loss												$ (9,142,624)
BALANCE, DECEMBER 31, 1999	11,158,546	32,540,145	433,638	4,336	396,839	6,027	(361)	—	(21,442)	(35,861,257)	(35,481,885)	
Exercise of stock options	—	—	24,618	246	24,791	—	—	—	—	—	25,037	
Sale of Series F Redeemable Convertible Preferred Stock, net of issuance costs of $1,309,965	6,325,329	28,735,348	—	—	—	—	—	—	—	—	—	
Sale of Series G Redeemable Convertible Preferred Stock	1,232,308	12,015,003	—	—	—	—	—	—	—	—	—	
Sale of Series H Redeemable Convertible Preferred Stock	1,127,819	7,499,996	—	—	—	—	—	—	—	—	—	

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS — (Continued)
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional Paid-in Capital	Treasury Stock		Accumulated Other Comprehensive Income	Deferred Stock-Based Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' (Deficit) Equity	Comprehensive Loss
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value		Number of Shares	Cost					
Issuance of restricted common stock for services performed	—	—	1,369	14	7,786	—	—	—	—	—	7,800	
Issuance of common stock for services performed	—	—	1,667	17	3,283	—	—	—	—	—	3,300	
Issuance of Series E Redeemable Convertible Preferred Stock warrants in connection with capital lease obligation	—	—	—	—	33,880	—	—	—	—	—	33,880	
Deferred stock-based compensation related to employees and nonemployees	—	—	—	—	162,442	—	—	—	(162,442)	—	—	
Amortization of deferred stock-based compensation	—	—	—	—	—	—	—	—	12,318	—	12,318	
Unrealized gain on short-term investments	—	—	—	—	—	—	—	16,511	—	—	16,511	$ 16,511
Accretion of dividends and offering costs on preferred stock	—	4,218,395	—	—	—	—	—	—	—	(4,218,395)	(4,218,395)	
Net loss	—	—	—	—	—	—	—	—	—	(24,428,759)	(24,428,759)	(24,428,759)
Comprehensive net loss												$(24,412,248)
BALANCE, DECEMBER 31, 2000	19,844,002	85,008,887	461,292	4,613	629,021	6,027	(361)	16,511	(171,566)	(64,508,411)	(64,030,193)	
Exercise of stock options	—	—	35,823	358	51,762	—	—	—	—	—	52,120	
Issuance of restricted common stock	—	—	13,790	138	347,539	—	—	—	(344,391)	—	3,286	
Sale of Series I Redeemable Convertible Preferred Stock, net of issuance costs of $27,345	1,370,324	6,481,694	—	—	—	—	—	—	—	—	—	
Issuance of Series F Redeemable Convertible Preferred Stock warrants in connection with facility lease	—	—	—	—	536,402	—	—	—	—	—	536,402	

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS — (Continued)
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional	Treasury Stock		Accumulated Other	Deferred	Deficit Accumulated During the	Total	
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value	Paid-in Capital	Number of Shares	Cost	Comprehensive Income	Stock-Based Compensation	Development Stage	Stockholders' (Deficit) Equity	Comprehensive Loss
Issuance of Series F Redeemable Convertible Preferred Stock warrants in connection with capital lease obligation	—	—	—	—	79,134	—	—	—	—	—	79,134	
Issuance of Series F Redeemable Convertible Preferred Stock warrants in connection with debt offering	—	—	—	—	594,698	—	—	—	—	—	594,698	
Deferred stock-based compensation related to employees and nonemployees	—	—	—	—	5,004,423	—	—	—	(5,004,423)	—	—	
Reversal of deferred compensation for terminated employees	—	—	—	—	(31,281)	—	—	—	31,281	—	—	
Amortization of deferred stock-based compensation	—	—	—	—	—	—	—	—	1,075,606	—	1,075,606	
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(12,942)	—	—	(12,942)	$ (12,942)
Accretion of dividends and offering costs on preferred stock	—	6,248,616	—	—	—	—	—	—	—	(6,248,616)	(6,248,616)	
Net loss	—	—	—	—	—	—	—	—	—	(18,277,192)	(18,277,192)	(18,277,192)
Comprehensive net loss												$(18,290,134)
BALANCE, DECEMBER 31, 2001	21,214,326	$ 97,739,197	510,905	$ 5,109	$ 7,211,698	6,027	$(361)	$ 3,569	$(4,413,493)	$ (89,034,219)	$(86,227,697)	
Exercise of stock options	—	—	8,560	86	29,028	—	—	—	—	—	29,114	
Sale of Series J Redeemable Convertible Preferred Stock, net of issuance costs of $856,034	10,736,960	14,283,074	—	—	—	—	—	—	—	—	—	
Exchange of Series B, E and F to Series J-1 for contribution greater than pro-rata share	3,232,930	—	—	—	—	—	—	—	—	—	—	
Conversion of preferred shares to common	(4,039,133)	(24,381,916)	699,411	6,994	24,374,922	—	—	—	—	—	24,381,916	
Reversal of deferred compensation for terminated employees	—	—	—	—	(424,887)	—	—	—	424,887	—	—	
Amortization of deferred stock-based compensation	—	—	—	—	—	—	—	—	2,195,202	—	2,195,202	
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(3,281)	—	—	(3,281)	$ (3,281)
Accretion of dividends and offering costs on preferred stock	—	6,665,478	—	—	—	—	—	—	—	(6,665,478)	(6,665,478)	

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS — (Continued)
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional	Treasury Stock		Accumulated Other	Deferred	Deficit Accumulated During the	Total	
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value	Paid-in Capital	Number of Shares	Cost	Comprehensive Income	Stock-Based Compensation	Development Stage	Stockholders' (Deficit) Equity	Comprehensive Loss
Dividends forfeited on preferred stock conversion	—	(2,838,758)	—	—	2,838,758	—	—	—	—	—	2,838,758	
Net loss	—	—	—	—	—	—	—	—	—	(21,896,250)	(21,896,250)	(21,896,250)
Comprehensive net loss												$(21,899,531)
BALANCE, DECEMBER 31, 2002	31,145,083	91,467,075	1,218,876	12,189	34,029,519	6,027	(361)	288	(1,793,404)	(117,595,947)	(85,347,716)	
Exercise of stock options	—	—	34,395	344	67,800	—	—	—	—	—	68,144	
Issuance of restricted common stock	—	—	14,956	150	102,149	—	—	—	(102,299)	—	—	
Warrants issued with convertible notes	—	—	—	—	761,500	—	—	—	—	—	761,500	
Retirement of treasury stock	—	—	(6,027)	(60)	(301)	(6,027)	361	—	—	—	—	
Conversion of preferred shares to common	(3,731,999)	(9,123,216)	732,600	7,326	9,115,890	—	—	—	—	—	9,123,216	
Amortization of deferred stock-based compensation	—	—	—	—	—	—	—	—	1,307,052	—	1,307,052	
Deferred stock-based compensation related to employees	—	—	—	—	1,396,347	—	—	—	(1,396,347)	—	—	
Reversal of deferred compensation	—	—	—	—	(261,769)		—	—	261,769	—	—	
Issuance of common stock from exercise of warrant	—	—	998	10	(10)	—	—	—	—	—	—	
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(288)	—	—	(288)	$ (288)

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' (DEFICIT) EQUITY, AND COMPREHENSIVE LOSS — (Continued)
Period from Inception (July 12, 1993) to December 31, 2003

	Redeemable Convertible Preferred Stock		Stockholders' (Deficit) Equity									
			Common Stock		Additional Paid-in Capital	Treasury Stock		Accumulated Other Comprehensive Income	Deferred Stock-Based Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' (Deficit) Equity	Comprehensive Loss
	Number of Shares	Carrying Value	Number of Shares	$0.01 Par Value		Number of Shares	Cost					
Accretion of dividends and offering costs on preferred stock	—	5,948,073	—	—	—	—	—	—	—	(5,948,073)	(5,948,073)	
Dividends forfeited on preferred stock conversion	—	(23,521,685)	—	—	23,521,685	—	—	—	—	—	23,521,685	
Issuance of common stock from initial public offering ("IPO"), net of offering costs	—	—	3,750,000	37,500	47,580,943	—	—	—	—	—	47,618,443	
Issuance of common stock from convertible notes payable and accrued interest, at IPO	—	—	2,411,846	24,118	20,400,152	—	—	—	—	—	20,424,270	
Conversion of preferred shares to common, at IPO	(27,413,084)	(64,770,247)	6,136,889	61,368	64,708,879	—	—	—	—	—	64,770,247	
Net loss	—	—	—	—	—	—	—	—	—	(21,923,437)	(21,923,437)	(21,923,437)
Comprehensive net loss												$(21,923,725)
BALANCE, DECEMBER 31, 2003	—	$ —	14,294,533	$142,945	$201,422,784	—	$ —	$ —	$(1,723,229)	$(145,467,457)	$ 54,375,043	

(Concluded)

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,			Period From Inception (July 12, 1993) to December 31,
	2001	2002	2003	2003
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net loss	$(18,277,192)	$(21,896,250)	$(21,923,437)	$(115,210,007)
Adjustments to reconcile net loss to net cash used in operating activities:				
Stock-based compensation expense	1,075,606	2,195,202	1,307,052	4,667,585
Depreciation and amortization	1,652,334	1,747,372	1,733,417	8,749,764
Noncash interest expense	186,050	383,698	1,120,526	1,969,268
Noncash rent expense	—	53,640	53,640	107,280
Equity in loss from joint venture	1,965,840	1,183,417	—	15,164,257
Changes in operating assets and liabilities:				
Due from joint venture	(2,371,572)	(777,685)	—	(3,149,257)
Other current assets	(243,070)	4,599	(283,836)	(829,934)
Accounts payable	333,148	(717,721)	782,267	1,519,983
Accrued expenses	(533,224)	141,585	1,703,194	2,922,939
Net cash used in operating activities	(16,212,080)	(17,682,143)	(15,507,177)	(84,088,122)
CASH FLOWS FROM INVESTING ACTIVITIES:				
Purchases of property and equipment	(47,153)	(686,613)	(534,713)	(1,777,598)
(Increase) decrease in other assets	(288,033)	(33,640)	(119,220)	(1,738,246)
Investment in joint venture	—	—	—	(12,015,000)
Maturities (purchases) of short-term investments	11,206,122	9,143,199	195,410	17,499
Net cash provided by (used in) investing activities	10,870,936	8,422,946	(458,523)	(15,513,345)
CASH FLOWS FROM FINANCING ACTIVITIES:				
Payments on long-term debt	(4,653,813)	(3,513,221)	(4,395,089)	(17,781,218)
Proceeds from long-term debt	5,000,000	—	19,440,342	29,440,342
Proceeds from financing of equipment	—	—	—	347,960
Net proceeds from sale of redeemable convertible preferred stock	6,481,694	14,283,074	—	94,337,203
Net proceeds from sale of common stock in initial public offering	—	—	47,618,443	47,618,443
Proceeds from exercise of stock options	55,406	29,114	68,144	202,475
Purchase of treasury stock	—	—	—	(1,360)
Net cash provided by financing activities	6,883,287	10,798,967	62,731,840	154,163,845

See notes to consolidated financial statements.

ACUSPHERE, INC. AND SUBSIDIARIES
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF CASH FLOWS — (Continued)

	Year Ended December 31,			Period From Inception (July 12, 1993) to December 31, 2003
	2001	2002	2003	
NET INCREASE IN CASH AND CASH EQUIVALENTS	1,542,143	1,539,770	46,766,140	54,562,378
CASH AND CASH EQUIVALENTS, Beginning of period	4,714,325	6,256,468	7,796,238	—
CASH AND CASH EQUIVALENTS, End of period	$ 6,256,468	$ 7,796,238	$ 54,562,378	$ 54,562,378
SUPPLEMENTAL SCHEDULE OF CASH FLOWS INFORMATION:				
Cash paid during the period for interest	$ 563,999	$ 916,048	$ 1,317,106	$ 4,735,941
SUPPLEMENTAL SCHEDULE OF NONCASH FINANCING TRANSACTIONS:				
Equipment acquired under capital lease obligations	$ 3,230,272	$ —	$ —	$ 8,894,983
Unrealized (loss) on investments	$ (12,942)	$ (3,281)	$ (288)	$ —
Warrant issued with facility lease	$ 536,402	$ —	$ —	$ 536,402
Discount on long-term debt and capital lease obligations	$ 673,832	$ —	$ —	$ 1,018,712
Deferred compensation for services to be performed	$ 5,340,204	$ —	$ 1,236,877	$ 6,768,885
Accretion of preferred stock dividends and offering costs	$ 6,248,616	$ 6,665,478	$ 5,948,073	$ 30,257,450
Dividends forfeited on preferred stock conversion	$ —	$ 2,838,758	$ 23,521,685	$ 26,360,443
Write-off of net amount due from joint venture	$ —	$ 371,953	$ —	$ 371,953
Warrants issued with convertible notes	$ —	$ —	$ 761,500	$ 761,500
Warrants exercised for common stock	$ —	$ —	$ 10	$ 10
Promissory notes and accrued interest converted into common stock, at IPO	$ —	$ —	$ 20,424,270	$ 20,424,270

(Concluded)

See notes to consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Operations

Acusphere, Inc. and Subsidiaries ("Acusphere" or the "Company") is a specialty pharmaceutical company that develops new drugs and improved formulations of existing drugs using its proprietary microparticle technology.

Acusphere is in the development stage and is devoting substantially all of its efforts towards the research and development of its product candidates and raising capital. Acusphere is subject to a number of risks similar to those of other development stage companies. Principal among these risks are the need to develop commercially usable products, competition from substitute products and larger companies, dependence on key individuals, and the need to obtain adequate financing necessary to fund product development.

2. Summary of Significant Accounting Policies

The accompanying consolidated financial statements reflect the application of certain accounting policies described below and elsewhere in the notes to the consolidated financial statements.

Principles of Consolidation — The accompanying consolidated financial statements include the amounts of Acusphere, Inc. and its two wholly owned subsidiaries, Acusphere Securities Corporation and Acusphere Newco, Ltd. Acusphere Securities Corporation was established in December 1996 as a Massachusetts securities corporation. Acusphere Newco, Ltd., as established in June 2000 by the Company and Elan Corporation, plc. ("Elan"), was 80.1% owned by the Company. In September 2002, the joint venture relationship was terminated at which time Acusphere Newco, Ltd. became a wholly owned subsidiary of the Company. In February 2003, Acusphere Newco, Ltd. was dissolved. The Company's investment in Acusphere Newco, Ltd. was accounted for under the equity method from inception through the termination date of the joint venture relationship and consolidated from that date through February 2003 (see Note 4). All intercompany balances and transactions have been eliminated in consolidation.

Stock Split — On September 12, 2003, the Company effected a 1-for-6 reverse stock split. All share and per share amounts in the consolidated financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

Use of Estimates — The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimated or assumed.

Cash, Cash Equivalents, and Short-Term Investments — Cash equivalents consist of short-term, highly liquid investments, including money market accounts, with original maturity dates of 90 days or less when purchased. Cash equivalents are carried at cost, which approximates their fair market value. Short-term investments at December 31, 2002 primarily consisted of investments in U.S. Treasury bonds that mature within one year from the date of purchase, are reported at fair value and are classified as available for sale.

Property and Equipment — Property and equipment are recorded at cost and depreciated over their estimated useful lives of three to five years using the straight-line method. Equipment under capital leases and leasehold improvements is depreciated over the remainder of the lease term. Acusphere reviews its property and equipment for impairment whenever events or changes in circumstances indicate that the

carrying value of certain assets might not be recoverable and recognizes a loss when it is probable that the estimated future cash flows will be less than the carrying value of the asset. Expenditures for maintenance and repairs are charged to expense as incurred.

Other Assets — Other assets consist of deposits to vendors for the manufacture of laboratory equipment, security deposits, and deferred rent expense.

Fair Value of Financial Instruments — The carrying amounts of Acusphere's financial instruments, which include cash equivalents, short-term investments, accounts payable, accrued expenses, and long-term obligations, approximate their fair values.

Concentrations of Credit Risk and Limited Suppliers — The financial instruments that potentially subject Acusphere to concentrations of credit risk are cash and cash equivalents. Acusphere's cash and cash equivalents are maintained with a highly rated commercial bank and its related investment management company.

Acusphere relies on certain materials used in its development process, each of which are available from limited sources. The failure of a supplier, including a subcontractor, to deliver on schedule could delay or interrupt the development process and thereby adversely affect Acusphere's operating results.

Research and Development Expenses — Research and development costs primarily consist of salaries and related expenses for personnel and capital resources. Other research and development expenses include fees paid to consultants and outside service providers and the costs of materials used in clinical trials and research and development. Acusphere charges all research and development expenses to operations as incurred, net of expenses reimbursed from third parties.

Income Taxes — Deferred tax liabilities and assets are provided for differences between the book and tax bases of existing assets and liabilities and tax loss carryforwards and credits, using tax rates expected to be in effect in the years in which differences are expected to reverse. Valuation allowances are provided to the extent realization of tax assets is not considered likely.

Stock-Based Compensation — Acusphere's employee stock option plan is accounted for using the intrinsic-value-based method of Accounting Principles Board ("APB") Opinion No. 25, "Accounting for Stock Issued to Employees," and related interpretations. The intrinsic method requires that compensation expense, if any, be determined by calculating the difference between the fair value of the Company's common stock and the strike price of the option at a measurement date. The measurement date is generally when the number of shares and the strike price of the option are known. Acusphere uses the fair-value method to account for nonemployee stock-based compensation.

Acusphere has computed the pro forma disclosures required under SFAS No. 123, "Accounting for Stock-Based Compensation," for options granted using the Black-Scholes option-pricing model prescribed by SFAS No. 123. The assumptions used and weighted-average information are as follows:

	December 31,		
	2001	2002	2003
Risk-free interest rate	3.54%-4.76%	3.22%-4.76%	2.53%-3.12%
Expected dividend yield	—	—	—
Expected lives	4 years	4 years	4 years
Expected volatility	60%	60%	60%-100%
Weighted-average fair value of options granted	$24.48	$4.38	$6.20

Had compensation cost for the plan been determined consistent with SFAS No. 123, Acusphere's net loss would have been the following pro forma amounts:

	Year Ended December 31,		
	2001	2002	2003
Applicable to common stockholders:			
Net loss — as reported	$(24,525,808)	$(28,561,728)	$(27,871,510)
Add: Stock-based compensation expense included in reported net loss	929,389	2,167,834	1,211,273
Deduct: Stock-based compensation expense determined under fair value method	(1,364,928)	(2,279,228)	(1,184,230)
Net loss — proforma	$(24,961,347)	$(28,673,122)	$(27,844,467)
Net loss per share (basic and diluted):			
As reported	$ (50.81)	$ (35.39)	$ (6.66)
Pro forma	$ (51.71)	$ (35.53)	$ (6.65)

Net Loss Per Share — Basic and diluted net loss per common share is calculated by dividing the net loss applicable to common stockholders by the weighted-average number of unrestricted common shares outstanding during the period. Diluted net loss per common share is the same as basic net loss per common share, since the effects of potentially dilutive securities are antidilutive for all periods presented. Antidilutive securities, which consist of redeemable convertible preferred stock, stock options, warrants, and restricted common stock that are not included in the diluted net loss per share calculation, aggregated 4,120,371, 7,853,360, and 1,758,029 as of December 31, 2001, 2002, and 2003, respectively. The following table reconciles the weighted-average common shares outstanding to the shares used in the computation of basic and diluted weighted-average common shares outstanding:

	Year Ended December 31,		
Historical	2001	2002	2003
Weighted-average common shares outstanding	490,330	816,720	4,191,321
Less weighted-average restricted common shares outstanding	(7,617)	(9,601)	(3,649)
Basic and diluted weighted-average common shares outstanding	482,713	807,119	4,187,672

Comprehensive Loss — Comprehensive loss is defined as the change in stockholders' (deficit) equity during a period from transactions and other events and circumstances from non-owner sources. Acusphere has disclosed comprehensive loss for all periods presented in the accompanying consolidated statements of redeemable convertible preferred stock, stockholders' (deficit) equity, and comprehensive loss.

Disclosures About Segments of an Enterprise — Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker, or decision-making group, in making decisions regarding resource allocation and assessing performance. To date, Acusphere has viewed its operations and manages its business as principally one operating segment.

Recently Issued Accounting Pronouncements — In January 2003, the Financial Accounting Standards Board issued Interpretation No. 46, "Consolidation of Variable Interest Entities" (FIN 46), which was amended by FIN 46R issued in December 2003. This interpretation of Accounting Research Bulletin No. 51, "Consolidated Financial Statements," addresses consolidation by business enterprises of variable interest entities (VIEs) that either: (1) do not have sufficient equity investment at risk to permit the

entity to finance its activities without additional subordinated financial support, or (2) for which the equity investors lack an essential characteristic of a controlling financial interest. This Interpretation applies immediately to VIEs created after January 31, 2003. It also applies in the first fiscal year or interim period ending after March 15, 2004, to VIEs created before February 1, 2003 in which an enterprise holds a variable interest. FIN 46 requires disclosure of VIEs in financial statements issued after January 31, 2003, if it is reasonably possible that as of the transition date: (1) the company will be the primary beneficiary of an existing VIE that will require consolidation or, (2) the company will hold a significant variable interest in, or have significant involvement with, an existing VIE. We are currently in the process of completing our review of the requirements of FIN 46. However, we have not yet identified any entities that require disclosure or entities that would require consolidation under FIN 46 that had not previously been consolidated as a result of FIN 46.

3. Balance Sheet Data

	As of December 31, 2002	As of December 31, 2003
Other assets consist of the following:		
Deposits	$1,647,038	$1,195,672
Other assets	515,158	429,125
	$2,162,196	$1,624,797
Accrued expenses consist of the following:		
Accrued contract services	$ 522,002	$ 882,696
Accrued vacation	315,771	316,644
Accrued bonus	—	350,000
Other accrued expenses	381,971	389,672
	$1,219,744	$1,939,012

4. Joint Venture

In June 2000, Acusphere and Elan formed a joint venture, Acusphere Newco, Ltd., to develop compounds to be delivered via the pulmonary route using Acusphere's microparticle technology.

The joint venture was formed by issuing preferred and common stock valued at $15,000,000 to Acusphere and Elan. Elan also purchased shares of Acupshere's Series G Nonvoting Redeemable Convertible Preferred Stock for total proceeds of $12,015,003. As discussed above and in Note 2, until September 30, 2002, Acusphere owned an 80.1% interest in the joint venture and Elan owned a 19.9% nonvoting interest. While Acusphere owned 100% of the voting common shares, Elan and its subsidiaries retained significant minority investor rights that were considered "participating rights" as defined in Emerging Issues Task Force ("EITF") Issue No. 96-16, "Investors' Accounting for an Investee When the Investor Has a Majority of the Voting Interest but the Minority Shareholder Has Certain Approval or Veto Rights." Elan's participating rights consisted of joint and equal participation with Acusphere in the joint venture's operating and capital decisions through equal representation and participation in the joint venture's management and research and development committees. Elan's participating rights overcame the presumption that Acusphere exercised control over the joint venture. Accordingly, Acusphere did not consolidate the financial statements of the joint venture but, instead, accounted for its investment in the joint venture under the equity method of accounting.

In conjunction with a private equity financing completed by Acusphere in July 2002, the preferred stock then held by Elan and carried at an aggregate value of $21,049,000 was converted into 419,575 shares of Acusphere common stock.

In September 2002, Elan and Acusphere terminated the joint venture agreement. This termination resulted in the assignment to Acusphere of development rights to any project undertaken by the joint venture since its formation in exchange for Elan's minority participation in certain revenues that may be realized in the future relating to technology developed by the joint venture. In connection with the termination of the joint venture, Acusphere recognized as a loss an amount previously due from Elan of $374,000. Upon termination of the joint venture, Acusphere Newco, Ltd. became a wholly owned subsidiary of Acusphere and was consolidated in the Company's financial statements until this subsidiary was dissolved in February 2003.

5. Long-Term Debt

The carrying value of long-term debt is as follows at December 31:

	2002	2003
Capital lease obligations	$2,342,045	$1,090,217
Subordinated loans payable	2,948,198	—
	5,290,243	1,090,217
Less current maturities	3,564,655	884,799
Long-term debt, net	$1,725,588	$ 205,418

Capital Lease Obligations — Acusphere leases capital equipment under various capital lease arrangements. The remaining monthly payments range from $3,708 to $46,222 with maturities through April 2005. As part of these and prior lease agreements entered into by the Company, the leasing companies were granted warrants to purchase an aggregate of 32,128 shares of common stock at a purchase price per share equal to the then-current fair value. In conjunction with these grants, Acusphere recorded the deemed fair value of these warrants as a reduction of the capital lease obligations based upon the Black-Scholes option-pricing model and is amortizing these discounts using the effective-interest-rate method through the respective maturity dates of the leases. Interest rates for the above leases range from 6.7% to 8.6%. Acusphere does not have any additional borrowing availability under these lease arrangements as of December 31, 2003.

Future payments under all capital lease agreements are as follows as of December 31, 2003:

Year Ending December 31,	
2004	$ 941,180
2005	208,524
Total future minimum lease payments	1,149,704
Less amount representing interest	59,487
Present value of future minimum lease payments	1,090,217
Less current portion of capital leases	884,799
Long-term portion of capital leases	$ 205,418

At December 31, 2003, the cost and net carrying value of equipment under capital leases amounted to approximately $2,549,000 and $905,000, respectively.

Subordinated Loans Payable — In September 2001, Acusphere entered into notes payable agreements (the "notes") with two financing institutions for a total amount of $5,000,000. The notes specified six monthly interest-only payments which began in October 2001 and 24 monthly principal and interest installments thereafter. The notes bore interest at 15% per annum. The balance of the notes was paid in full in 2003.

In conjunction with the issuance of the notes, Acusphere issued warrants to purchase an aggregate of 28,138 shares of common stock for $650,000, subject to adjustment under certain circumstances, as defined. Based on the relative value of the notes and the deemed value of the warrants, Acusphere allocated a total of $594,698 of proceeds to the warrants. The carrying value of the notes was reduced by the unamortized discount. Acusphere has amortized this discount using the effective-interest-rate method through June 2003 when the debt was repaid in full. During 2001, 2002 and 2003, Acusphere recorded $87,617, $330,279 and $176,802, respectively of interest expense relating to the amortization of the discount on the notes.

Convertible Promissory Notes — On April 11, 2003, the Company issued subordinated convertible promissory notes to existing investors in exchange for $19,100,000. The notes bore interest at a rate of 10% per annum. On June 27, 2003, the Company issued identical subordinated convertible promissory notes to other existing investors in exchange for an additional $319,000. The outstanding balance of the notes and accrued interest automatically converted into common stock on October 14, 2003 upon the close of the initial public offering ("IPO") of the Company's Common Stock. The secured subordinated convertible promissory notes, including accrued interest, were converted at an effective price of $8.46 per share into 2,411,846 shares of common stock. At December 31, 2003, none of these convertible promissory notes were outstanding and the security interest previously held by the noteholders was released.

In connection with the issuance of the subordinated convertible promissory notes, for no additional consideration, the Company issued warrants exercisable for 458,437 shares of common stock at an exercise price of $8.46 per share and 684 shares of common stock at an exercise price of $14.00 per share (see Note 8). Based on the relative value of the notes and the deemed value of the warrants, the Company allocated $761,500 of the proceeds to the warrants. The carrying value of the notes was reduced by the unamortized discount. As a result of the IPO on October 14, 2003, the discount was fully amortized into interest expense during 2003.

6. Income Taxes

At December 31, 2003, Acusphere had a net operating loss ("NOL") carryforward for income tax purposes of approximately $68,528,000 that expires through 2023. Acusphere also has approximately $2,555,000 of research and development ("R&D") credits as of December 31, 2003 available to offset future income taxes payable, if any. The Tax Reform Act of 1986 contains provisions that may limit the utilization of NOL carryforwards and R&D credits available to be used in any given year in the event of significant changes in ownership interests, as defined.

The components of Acusphere's deferred tax asset at December 31, 2002 and 2003 are as follows:

	2002	2003
Net operating loss carryforwards	$ 22,321,000	$ 26,610,000
Joint venture loss	6,066,000	—
Temporary timing differences	7,645,000	11,406,000
Research and development credit carryforwards	2,119,000	2,555,000
Deferred tax asset	38,151,000	40,571,000
Less valuation allowance	(38,151,000)	(40,571,000)
	$ —	$ —

The net operating loss carryforward associated with the joint venture expired when Acusphere Newco, Ltd. (a Bermuda company) was liquidated in February 2003 and, accordingly, the deferred tax asset was eliminated.

The temporary differences principally consist of capitalized start-up expenses for income tax purposes. Acusphere has established a full valuation allowance equal to the amount of its deferred tax asset as the realization of such asset is uncertain.

7. Stockholders' (Deficit) Equity

Common Stock — On October 14, 2003, the Company's Registration Statement on Form S-1, as amended, was declared effective by the Securities and Exchange Commission permitting the Company to sell shares of common stock in an IPO. On October 7, 2003, the Company sold 3,750,000 shares of common stock in the IPO for $14.00 per share which resulted in net proceeds of approximately $47,600,000 to the Company, after deducting $4,900,000 in underwriting fees and offering-related expenses.

Holders of common stock are entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Holders of common stock are entitled to receive ratably any dividends as may be declared by the Company's Board of Directors.

Conversions to Common Stock — On June 17, 2002, in connection with the Series J preferred stock financing, 4,039,133 shares of outstanding preferred stock were converted into 699,411 shares of common stock. On July 1, 2003, in connection with the issuance of the subordinated convertible promissory notes, 3,731,999 shares of outstanding preferred stock converted into 732,600 shares of common stock. At the IPO, all the remaining 27,413,084 outstanding shares of preferred stock and all of the Company's outstanding subordinated convertible promissory notes, including accrued interest, converted into 8,548,735 shares of common stock.

Stock Plans — In March 1994, the 1994 Stock Plan (the "1994 Plan") was approved. The 1994 Plan, as amended provides that a maximum of 1,423,663 shares of common stock may be issued as incentive stock options ("ISOs"), nonqualified stock options and stock grants. Options under the Plan may be granted to key employees, directors, and consultants, as defined. ISOs may be granted at no less than fair market value on the date of grant, as determined by the Company's Board of Directors (no less than 110% of fair market value on the date of grant for 10% or greater stockholders), subject to certain limitations, as defined. Options granted under the Plan are exercisable at varying dates, as determined by the Board of Directors, and have terms not to exceed 10 years (five years for 10% or greater stockholders). The Board of Directors, at the request of the optionee, may, at its discretion, convert the optionee's ISOs into nonqualified options at any time prior to the expiration of such ISOs. The Company had 77,809 shares

available for future stock and option grants under the Plan at December 31, 2003. No new stock options or other stock grants can be made by the Company under the 1994 Plan after March 7, 2004.

In July 2003, the 2003 Stock Option and Incentive Plan (the "2003 Plan") was approved. The 2003 Plan became effective on the closing of IPO on October 14, 2003 and provides that a maximum of 2,500,000 shares of common stock may be issued as ISOs, nonqualified stock option, awards of common stock and direct purchases of common stock by Acusphere employees, officers, directors and consultants. The maximum number of shares that may be granted to any employee under the 2003 shall not exceed 583,334 shares of common stock during any calendar year. Acusphere had 2,500,000 shares available for future stock and option grants under the 2003 Plan at December 31, 2003.

In July 2003, the 2003 Employee Stock Purchase Plan was approved which became effective on October 14, 2003, the close of the Company's initial public offering. The purchase plan provides for the issuance of a maximum of 233,334 shares of common stock. Eligible employee may contribute up to 10% of their total cash compensation with a maximum of 417 shares semi-annually. The first sale of shares under this plan occurred on February 29, 2004.

As of December 31, 2003, no stock option activity had occurred under the 2003 Plan. Stock option activity under the 1994 Plan was as follows:

	Number of Shares	Exercise Price Per Share	Weighted-Average Exercise Price Per Share
Balance, December 31, 1995	61,176	$0.60 - $ 1.02	$0.66
Granted	23,976	0.96 - 1.26	1.08
Exercised	(1,736)	0.60 - 0.96	0.66
Canceled	(598)	0.60 - 0.96	0.90
Balance, December 31, 1996	82,818	0.60 - 1.26	0.78
Granted	76,799	1.26 - 1.80	1.44
Exercised	(352)	0.60	0.60
Balance, December 31, 1997	159,265	0.60 - 1.80	1.08
Granted	64,871	1.80 - 1.98	1.86
Exercised	(6,570)	0.60 - 1.80	0.72
Canceled	(12,079)	0.60 - 1.98	1.74
Balance, December 31, 1998	205,487	0.60 - 1.98	1.32
Granted	30,987	1.98	1.98
Exercised	(3,500)	0.60 - 1.80	0.66
Canceled	(18,646)	1.80 - 1.98	1.80
Balance, December 31, 1999	214,328	0.60 - 1.98	1.38
Granted	81,101	1.98 - 5.70	4.20
Exercised	(24,618)	0.60 - 1.98	1.02
Canceled	(27,697)	1.26 - 1.98	1.92

	Number of Shares	Exercise Price Per Share	Weighted-Average Exercise Price Per Share
Balance, December 31, 2000	243,114	0.60 - 5.70	2.28
Granted	230,119	5.70 - 7.20	7.20
Exercised	(35,823)	0.60 - 7.20	1.44
Canceled	(12,928)	1.80 - 7.20	4.32
Balance, December 31, 2001	424,482	0.60 - 7.20	5.34
Granted	366,429	0.84 - 7.20	1.68
Exercised	(8,560)	0.84 - 7.20	3.42
Canceled	(18,421)	0.84 - 7.20	5.88
Balance December 31, 2002	763,930	0.60 - 7.20	3.36
Granted	505,072	0.84 - 13.02	8.00
Exercised	(34,395)	0.60 - 7.20	1.98
Canceled	(62,645)	0.84 - 7.20	6.71
Balance, December 31, 2003	1,171,962	$0.60 - $13.02	5.23
Exercisable, December 31, 2003	443,048	$0.60 - $13.02	$3.63
Exercisable, December 31, 2002	285,494	0.60 - 7.20	3.48
Exercisable, December 31, 2001	181,713	0.60 - 7.20	2.64
Exercisable, December 31, 2000	176,144	0.60 - 5.70	1.02

The following table summarizes information relating to currently outstanding and exercisable options as of December 31, 2003 as follows:

	Outstanding			Exercisable	
Exercise Price	Number of Shares	Weighted-Average Remaining Contractual Life (in Years)	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price
$0.60 - $ 0.84	517,993	8.8	$ 0.84	160,909	$0.83
0.96 - 1.26	45,596	2.7	1.17	45,596	1.17
1.80 - 2.82	68,123	5.5	1.92	67,897	1.92
$5.70 - $13.02	540,250	8.9	10.20	168,646	7.67
	1,171,962			443,048	

Grants Resulting in Stock-based Compensation Expense — In 2000, the Company issued 1,667 shares of common stock, 1,369 shares of restricted common stock, and 10,000 options to purchase common stock to non-employees in consideration of services rendered. During 2001 and 2003, the Company issued 13,791 and 14,956 shares, respectively, of restricted common stock to a non-employee and certain directors in consideration of services rendered. These shares of restricted common stock vest ratably from 6 to 48 months from their respective dates of issuance. Acusphere has the right to repurchase the unvested portion of the restricted common stock at the original issue price upon certain events. Acusphere recorded these issuances of securities (stock options and restricted stock) at fair value at date of grant, which was $53,822, $419,594 and $102,299 in 2000, 2001 and 2003, respectively, and is recording stock-based

compensation over the vesting periods. Pursuant to EITF Issue No. 96-18, "Accounting for Equity Instruments Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services," Acusphere must periodically remeasure the fair value of unvested non-employee equity instruments through the earlier of a performance commitment or performance completion, as defined in EITF Issue No. 96-18. The periodic remeasurement of the fair value may result in additional charges to operations in future periods.

Acusphere issued options to employees to purchase approximately 230,119, and 267,723 shares of common stock during the years ended December 31, 2001 and 2003, respectively, at exercise prices deemed for accounting purposes to be below market value. Acusphere has recorded the difference between the exercise price and the fair value of $4,884,975 in 2001 and $1,396,347 in 2003 as deferred stock-based compensation and is amortizing this deferred compensation as charges to operations over the vesting periods of the options. Acusphere expects to record approximately $786,000, $481,000, $324,000 and $25,000 of stock-based compensation expense related to the amortization of deferred compensation for the years ending December 31, 2004, 2005, 2006 and 2007, respectively.

8. Convertible Preferred Stock and Warrants

During 2002 and 2003, all shares of the Company's outstanding preferred stock were converted into common stock. These conversions were made based upon conversion ratios defined for each series of preferred stock. There were no outstanding shares of preferred stock at December 31, 2003. In connection with the Company's IPO, all remaining outstanding shares of preferred stock converted to common stock. Prior to the IPO, sales of preferred stock provided the primary source of funding for the Company. The following table summarized the activity for the convertible preferred stock.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

	Series A Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Series D Preferred Stock		Series E Preferred Stock		Series F Preferred Stock		Series G Preferred Stock		Series H Preferred Stock		Series I Preferred Stock		Series J Preferred Stock		Series J-1 Preferred Stock	
	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value
Inception of Company (July 12, 1993):																						
Sale of Series A Preferred Stock, net of issuance costs of $26,813	775,000	$ 748,187	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —
Accretion of offering costs	—	1,957	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1994	775,000	750,144	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Sale of Series B Preferred Stock, net of issuance costs of $45,024	—	—	2,265,625	3,579,976	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of preferred stock for services	41,169	41,169	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Accretion of offering costs	—	2,389	—	2,666	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1995	816,169	793,702	2,265,625	3,582,642	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Sale of Series C Preferred Stock, net of issuance costs of $44,915	—	—	—	—	3,913,551	8,330,084	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Accretion of dividends and offering costs	—	2,389	—	4,505	—	713,121	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1996	816,169	796,091	2,265,625	3,587,147	3,913,551	9,043,205	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Sale of Series D Preferred Stock, net of issuance costs of $39,895	—	—	—	—	—	—	3,405,624	10,176,977	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Accretion of dividends and offering costs	—	2,389	—	4,505	—	1,257,339	—	171,027	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1997	816,169	798,480	2,265,625	3,591,652	3,913,551	10,300,544	3,405,624	10,348,004	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Sale of Series E Preferred Stock, net of issuance costs of $13,140	—	—	—	—	—	—	—	—	757,577	2,486,864	—	—	—	—	—	—	—	—	—	—	—	—
Accretion of dividends and offering costs	—	2,389	—	4,505	—	1,257,339	—	1,095,078	—	51,567	—	—	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1998	816,169	800,869	2,265,625	3,596,157	3,913,551	11,557,883	3,405,624	11,443,082	757,577	2,538,431	—	—	—	—	—	—	—	—	—	—	—	—
Accretion of dividends and offering costs	—	2,389	—	4,505	—	1,257,339	—	1,095,078	—	244,412	—	—	—	—	—	—	—	—	—	—	—	—

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

	Series A Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Series D Preferred Stock		Series E Preferred Stock		Series F Preferred Stock		Series G Preferred Stock		Series H Preferred Stock		Series I Preferred Stock		Series J Preferred Stock		Series J-1 Preferred Stock	
	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value	Number of Shares	Carrying Value
Balance, December 31, 1999	816,169	803,258	2,265,625	3,600,662	3,913,551	12,815,222	3,405,624	12,538,160	757,577	2,782,843	—	—	—	—	—	—	—	—	—	—	—	—
Sale of Series F Preferred Stock, net of issuance costs of $1,309,965	—	—	—	—	—	—	—	—	—	—	6,325,329	28,735,348	—	—	—	—	—	—	—	—	—	—
Sale of Series G Preferred Stock, net of issuance costs of $0	—	—	—	—	—	—	—	—	—	—	—	—	1,232,308	12,015,003	—	—	—	—	—	—	—	—
Sale of Series H Preferred Stock, net of issuance costs of $0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1,127,819	7,499,996	—	—	—	—	—	—
Accretion of dividends and offering costs	—	2,389	—	4,505	—	1,257,339	—	1,095,078	—	244,412	—	1,073,766	—	360,455	—	180,451	—	—	—	—	—	—
Balance, December 31, 2000	816,169	805,647	2,265,625	3,605,167	3,913,551	14,072,561	3,405,624	13,633,238	757,577	3,027,255	6,325,329	29,809,114	1,232,308	12,375,458	1,127,819	7,680,447	—	—	—	—	—	—
Sale of Series I Preferred Stock, net of issuance costs of $27,345	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1,370,324	6,481,694	—	—	—	—
Accretion of dividends and offering costs	—	2,389	—	4,505	—	1,257,339	—	1,095,078	—	244,412	—	2,281,585	—	742,528	—	360,901	—	259,879	—	—	—	—
Balance, December 31, 2001	816,169	808,036	2,265,625	3,609,672	3,913,551	15,329,900	3,405,624	14,728,316	757,577	3,271,667	6,325,329	32,090,699	1,232,308	13,117,986	1,127,819	8,041,348	1,370,324	6,741,573	—	—	—	—
Sale of Series J Preferred Stock, net of issuance costs of $856,034	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	10,736,960	14,283,074	—	—
Conversion of preferred shares to common shares	(250,359)	(250,359)	(689,949)	(1,103,920)	(431,612)	(923,650)	(167,182)	(501,548)	(76,536)	(252,570)	(47,544)	(225,836)	(1,232,308)	(13,548,873)	(1,127,819)	(7,499,996)	(15,824)	(75,164)				
Exchange of Series B, E and F to Series J-1 for contribution greater than pro-rata share	—	—	(31,250)	(50,000)	—	—	—	—	(31,742)	(104,749)	(1,345,061)	(6,389,038)	—	—	—	—	—	—	—	—	4,640,983	6,543,787
Write-off of forfeited dividends	—	—	—	—	—	(876,524)	—	(247,155)	—	(110,107)	—	(856,359)	—	—	—	(743,310)	—	(5,303)	—	—	—	—
Accretion of dividends and offering costs	—	2,538	—	4,776	—	1,236,058	—	1,066,670	—	208,707	—	2,067,771	—	430,887	—	201,958	—	442,892	—	728,113	—	275,108
Balance, December 31, 2002	565,810	$ 560,215	1,544,426	$ 2,460,528	3,481,939	$14,765,784	3,238,442	$15,046,283	649,299	$ 3,012,948	4,932,724	$26,687,237	—	$ —	—	$ —	1,354,500	$ 7,103,998	10,736,960	$ 15,011,187	4,640,983	$ 6,818,895
Conversion of preferred shares to common shares	—	—	(218,750)	(350,000)	(140,187)	(300,000)	(1,819,209)	(5,457,627)	(145,263)	(479,368)	(116,500)	(553,375)	—	—	—	—	(48,203)	(228,964)	(1,074,156)	(1,514,561)	(169,731)	(239,321)
Write-off of forfeited dividends	—	—	—	—	—	(8,189,466)	—	(5,989,123)	—	(1,024,807)	—	(5,093,707)	—	—	—	—	—	(1,022,713)	—	(1,530,770)	—	(671,099)
Accretion of dividends and offering costs	—	5,593	—	10,555	—	875,034	—	658,167	—	154,543	—	1,836,914	—	—	—	—	—	352,583	—	1,658,693	—	395,991
Conversion of preferred shares to common shares in IPO	(565,810)	(565,808)	(1,325,676)	(2,121,083)	(3,341,752)	(7,151,352)	(1,419,233)	(4,257,700)	(504,036)	(1,663,316)	(4,816,224)	(22,877,069)	—	—	—	—	(1,306,297)	(6,204,904)	(9,662,804)	(13,624,549)	(4,471,252)	(6,304,466)
Balance, December 31, 2003	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —

(Concluded)

Common Stock Warrants — As of December 31, 2003, warrants to purchase shares of the Company's stock, the origination of which were derived from debt and lease financing transactions, were outstanding for an aggregate of 573,842 shares of common stock at an effective weighted average price of $10.67 per shares as follows:

Number of Shares	Exercise Price Per Share	Expiration Date
1,066	$ 9.30	May 1, 2005
4,724	11.64	August 21, 2006
7,517	11.64	June 6, 2007
5,194	23.10	February 21, 2008
3,404	15.42	February 26, 2008
450,897	8.46	April 11, 2008
684	14.00	April 11, 2008
7,540	8.46	June 27, 2008
16,212	15.42	October 16, 2008
14,934	16.74	October 19, 2008
2,688	16.74	January 5, 2010
30,844	23.10	March 30, 2011
28,138	23.10	September 27, 2011
573,842		

During 2003, warrants were exercised at $9.30 per share resulting in the issuance of 998 shares of common stock.

9. Research and License Agreements

Acusphere has clinical and pre-clinical study research agreements with various institutions. Total expenses incurred amounted to approximately $2,761,000, $1,350,000 and $1,818,000 in sponsored-research expenses relating to such agreements during the years ended December 31, 2001, 2002, and 2003, respectively.

10. Commitments

Operating Leases — Acusphere has leased office and laboratory space under various agreements classified as operating leases. During 2001, 2002, and 2003, rent expense totaled approximately $1,349,000, $2,601,000, and $2,473,000, respectively.

Acusphere operates from a facility under a 10-year lease which began in December 2001. Acusphere is required to maintain a security deposit totaling $997,500 as a condition of this lease. This deposit amount is included in other assets at December 31, 2002 and 2003. In conjunction with the lease agreement, Acusphere issued a warrant to the lessor which allows for the purchase of 30,844 shares of common stock. Acusphere recorded the deemed fair value of the warrant of $536,402, based upon the Black-Scholes option-pricing model, as a deferred rent expense included in other assets, which is being amortized over the lease term as rent expense. $0, $53,640 and $53,640 of amortization has been recorded within rent expense as of December 31, 2001, 2002 and 2003, respectively.

Future minimum payments due under the noncancelable facility lease are as follows as of December 31, 2003:

Year Ending December 31,	
2004	$ 2,145,000
2005	2,220,000
2006	2,298,000
2007	2,379,000
2008	2,462,000
Thereafter	7,915,000
	$19,419,000

11. Employee Benefit Plan

Acusphere has a 401(k) profit sharing plan covering all employees of the Company who meet certain defined requirements. Under the terms of the 401(k) plan, the employees may elect to make tax-deferred contributions up to 20% of their salaries, subject to certain limitations as defined by the Internal Revenue Code. The Company does not make any matching contributions to the 401(k) plan and employees are not eligible to invest directly in shares of Acusphere's stock under this plan.