PROSPECTUS

3,750,000 Shares

ACUSPHERE

Common Stock

We are selling 3,750,000 shares of common stock. This is an initial public offering of shares of our common stock. Prior to this offering, there has been no public market for our common stock. See "Underwriting" for a discussion of the factors considered in determining the initial public offering price. Our common stock has been approved for quotation on the Nasdaq National Market under the symbol "ACUS" subject to official notice of issuance.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page 5 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	**$14.00**	**$52,500,000**
Underwriting discounts and commissions	**$ 0.98**	**$ 3,675,000**
Proceeds, before expenses, to us	**$13.02**	**$48,825,000**

The underwriters may also purchase up to 562,500 shares of our common stock from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments.

The underwriters expect to deliver the shares in New York, New York on or about October 14, 2003.

SG Cowen

Thomas Weisel Partners LLC

U.S. Bancorp Piper Jaffray

Friedman Billings Ramsey

October 7, 2003

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

Until November 1, 2003, all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

The names "Acusphere," "HDDS" and "PDDS" and our logo are our trademarks. This prospectus also contains the trademarks and tradenames of other entities that are the property of their respective owners.

PROSPECTUS SUMMARY

The following summary is qualified in its entirety by, and should be read in conjunction with, the more detailed information and consolidated financial statements and notes thereto appearing elsewhere in this prospectus. Before you decide to invest in our common stock, you should read the entire prospectus carefully, including the risk factors and consolidated financial statements and related notes included in this prospectus. Unless otherwise indicated, all information in this prospectus assumes no exercise of the underwriters' over-allotment option.

Our Company

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 microparticles in a versatile manner, so we can customize the microparticles to address the delivery needs of a variety of drugs. We are focused on creating porous microparticles that are smaller than red blood cells. 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.

Our Proprietary Product Candidates

AI-700, Intravenous Delivery of Gas for Ultrasound Contrast. We designed AI-700 to assess blood flow to the heart muscle, or myocardial perfusion, which is a sensitive marker for coronary artery disease. The current standard for assessing myocardial perfusion is a nuclear stress test, which is expensive, not widely available and time consuming and which exposes the patient and medical staff to radiation. Stress echocardiography, or ultrasound of the heart, is relatively inexpensive, more broadly available, fast and radiation-free, but detects wall motion abnormalities, which are downstream consequences of inadequate perfusion. Without a contrast agent, stress echo is incapable of assessing myocardial perfusion directly. Currently, there is no ultrasound contrast agent for myocardial perfusion assessment approved by the U.S. Food and Drug Administration, or FDA. We believe the cardiac indication for an ultrasound contrast agent capable of myocardial perfusion assessment could address a $1.9 billion potential market in the United States. AI-700 is an ultrasound contrast agent that is comprised of hollow microparticles containing gas, an effective reflector of ultrasound. AI-700 acts as a tracer of abnormal blood flow, which is associated with many life-threatening diseases, such as coronary artery disease. Future indications may exist for other diseases associated with abnormal blood flow, such as cancer, renal artery disease and peripheral vascular disease. Based on our Phase II studies, we believe stress echo with AI-700 has the potential to obtain information comparable to the nuclear stress test. We also believe stress echo with AI-700 can offer cost and convenience advantages over the nuclear stress test. We began enrollment in a Phase III program in early 2003.

AI-850, First Clinical-Stage Product Candidate from Our Hydrophobic Drug Delivery System, HDDS. Drugs that do not dissolve well in water, or hydrophobic drugs, are often difficult to formulate, especially for intravenous delivery. AI-850 is an improved formulation of paclitaxel, a hydrophobic drug that is the active ingredient in Taxol, a leading cancer drug that generated revenues of $857 million in 2002. To dissolve paclitaxel, Taxol contains Cremophor, which is believed to cause severe hypersensitivity reactions. We have increased the dissolution rate of paclitaxel by converting it into small sponge-like microparticles

thereby increasing the surface available for interaction with water. AI-850 is a Cremophor-free, readily dissolvable formulation of paclitaxel that can be delivered intravenously. AI-850 is currently being evaluated in a Phase I clinical trial at higher doses of paclitaxel than those customarily delivered with Taxol using the same dosing schedule for the treatment of metastatic breast cancer. In addition to paclitaxel, we have demonstrated that our HDDS technology improves the dissolution rate of a variety of hydrophobic drugs, including COX-2 inhibitors, taxanes, calcium channel blockers and anti-fungals.

AI-128, First Clinical-Stage Product Candidate from Our Pulmonary Drug Delivery System, PDDS. Many inhaled respiratory drugs are immediate release formulations that must be inhaled multiple times per day, and deliver peak and trough drug levels that may cause increased toxicity or reduced efficacy. AI-128 is a sustained release formulation of an FDA-approved, immediate release asthma drug with revenues in excess of $500 million in 2002. AI-128 is comprised of slowly dissolving microparticles with an appropriate size and porosity to enable them to be targeted to the upper lung, where the asthma drug can be released with reduced systemic exposure. The FDA-approved formulation must be inhaled multiple times per day, which discourages patient compliance. Non-compliance can lead to complications that result in increased emergency room visits and hospitalization. We believe AI-128 may allow patients to take treatments less frequently, and may offer improved performance through moderation of peak and trough drug levels associated with the FDA-approved formulation of the drug. We have completed a Phase I clinical trial for AI-128 that demonstrated targeted delivery to the upper lung and sustained release of the drug for up to 24 hours. Many inhaled respiratory drugs are immediate release formulations that could potentially benefit from our PDDS technology.

Our Strategy

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 intend to complete Phase III trials for AI-700 and submit a New Drug Application, or NDA, to the FDA by the end of 2005.
- *Focus on Proprietary Product Opportunities.* We intend to focus on proprietary product opportunities where we own broad patent rights to the products. We may develop and commercialize some of these products on our own in markets we can readily address. In other markets, we may establish collaborations with large pharmaceutical and biotechnology companies to enhance the development and commercialization of our product candidates.
- *Apply Our Proprietary Technology as a Delivery System for Patented Drugs.* Many patented drugs owned by large pharmaceutical companies are hydrophobic or delivered by inhalation. We plan to seek collaborations with companies that have patented drugs that could benefit from the most compelling capabilities of our HDDS and PDDS technologies.
- *Focus on Large Markets Where Our Product Candidates Can Address Significant Unmet Clinical Needs.* We intend to focus on drug candidates that we believe address large market opportunities where our porous microparticle technology can provide compelling clinical advantages over current products and approaches.

Corporate Information

We were organized as a Delaware corporation on July 12, 1993. Our principal executive offices are located at 500 Arsenal Street, Watertown, Massachusetts 02472. Our telephone number at that location is (617) 648-8800. Our website is located at www.acusphere.com. The information contained on our website is not part of this prospectus.

The Offering

Common stock offered hereby	3,750,000 shares
Common stock to be outstanding after the offering	14,270,797 shares
Use of proceeds	For research and development activities, including clinical trials for our lead product candidate, AI-700, and other product candidates, as well as working capital and other general corporate purposes. See "Use of Proceeds."
Proposed Nasdaq National Market symbol	ACUS

The above information is based on shares outstanding as of September 5, 2003 and excludes:

- 1,161,828 shares issuable upon exercise of options then outstanding at a weighted average exercise price of $5.19 per share;
- 581,825 shares issuable upon exercise of warrants then outstanding at a weighted average exercise price of $10.64 per share; and
- 89,605 shares issuable upon exercise of a purchase option then outstanding at an exercise price of $16.74 per share, which purchase option will expire upon completion of the offering made by this prospectus.

Unless otherwise noted, this prospectus:

- gives effect on a retroactive basis to a reverse split of our common stock of one share for each six shares of outstanding common stock effected on September 12, 2003;
- assumes no exercise of the underwriters' over-allotment option; and
- assumes the conversion of all of our outstanding convertible preferred stock and our outstanding 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, into 8,527,165 shares of our common stock upon the closing of this offering.

Summary Consolidated Financial Data
(in thousands, except per share data)

	Year Ended December 31,					Six Months Ended June 30,	
	1998	1999	2000	2001	2002	2002	2003
Statement of Operations Data:							
Research and development expense	$ 8,190	$ 7,022	$ 9,978	$ 11,536	$ 13,545	$ 7,426	$ 6,248
General and administrative expense	1,429	1,622	2,517	3,893	3,906	1,825	1,855
Stock-based compensation expense	—	5	16	1,076	2,195	1,122	712
Total operating expenses	9,619	8,649	12,511	16,505	19,646	10,373	8,815
Equity in loss of joint venture	—	—	(12,015)	(1,965)	(1,183)	(808)	—
Net loss	(9,415)	(9,141)	(24,429)	(18,277)	(21,896)	(11,774)	(9,907)
Net loss available to common stockholders	(11,826)	(11,745)	(28,647)	(24,526)	(28,562)	(15,058)	(13,142)
Net loss per diluted share	(28.32)	(27.24)	(64.20)	(50.82)	(35.40)	(30.24)	(10.87)
Weighted average diluted common shares outstanding	418	432	446	483	807	498	1,209

	As of June 30, 2003	
	Actual	As Adjusted
Balance Sheet Data:		
Cash and cash equivalents	$ 15,624	$ 62,949
Working capital	(5,953)	60,640
Total assets	20,405	67,730
Long-term debt, net of current portion	644	644
Convertible preferred stock	94,702	—
Total stockholders' equity (deficit)	(97,014)	64,280

The preceding table presents a summary of our balance sheet data as of June 30, 2003:

- on an actual basis;
- on an as adjusted basis to give effect to (a) the conversion on July 1, 2003 of 3,731,999 shares of our preferred stock into 732,600 shares of our common stock in connection with the issuance of our 10% convertible promissory notes, (b) the conversion of all of our remaining outstanding convertible preferred stock and our outstanding 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, into 8,527,165 shares of our common stock upon the closing of this offering, and (c) the sale of 3,750,000 shares of common stock by us in this offering at the initial offering price of $14.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses.

RISK FACTORS

An investment in our common stock involves significant risks. You should carefully consider the following risk factors before you decide to buy our common stock.

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 June 30, 2003, our cumulative net loss was $103.2 million. Our net loss was $21.9 million for the full year 2002 and $9.9 million for the first six months of 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. 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, together with proceeds from this offering, 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 and manufacture and distribution of 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 contract 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.

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 Photogen 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. 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 and Protarga, 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, two of which contain the active ingredient that is currently the subject of our research and development efforts, 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 have been 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 will be 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, contract 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 $46,000 in 2002 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.

Prior to this offering, you could not buy or sell our common stock publicly. An active public market for our common stock may not develop or be sustained after this offering. We have determined the initial public offering price with the representatives of the underwriters based on several factors. This price may vary from the market price of our common stock after this offering. You may be unable to sell

your shares of common stock at or above the initial offering price. 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 after this offering, 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. The lock-up agreements delivered by our executive officers and directors and substantially all of our stockholders and optionholders provide that SG Cowen Securities Corporation, in its sole discretion, may release those parties, at any time or from time to time and without notice, from their obligation not to dispose of shares of common stock for a period of 180 days after the date of this prospectus. 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. Please see "Shares Eligible for Future Sale."

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

After this offering, our directors and executive officers and their affiliates will collectively control approximately 44.4% of our outstanding common stock. 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.

Our management will have broad discretion as to the use of proceeds of this offering.

Our management will have broad discretion as to how the net proceeds of this offering will be used. Investors will be relying on the judgment of management regarding the application of the proceeds of this offering. The results and effectiveness of the application of the proceeds are uncertain.

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.

Certain of our financial statements have been audited by Arthur Andersen LLP, and the ability to recover damages from Arthur Andersen may be limited.

Prior to June 7, 2002, Arthur Andersen LLP served as our independent public accountants. On March 14, 2002, Arthur Andersen was indicted on federal obstruction of justice charges arising from the government's investigation of the Enron Corporation. On June 15, 2002, Arthur Andersen was convicted of those charges and the firm ceased practicing before the SEC on August 31, 2002.

Our inability to obtain the consent of Arthur Andersen to include its report on certain financial statements audited by Arthur Andersen and included in this prospectus may limit your recovery against Arthur Andersen under the securities laws. SEC rules require us to present in this prospectus certain historical financial statements for the year ended December 31, 2000 that were audited by Arthur Andersen. Since our former engagement partner and audit manager have left Arthur Andersen and Arthur Andersen has ceased its SEC practice, we have not been able to obtain the consent of Arthur Andersen to the inclusion of its audit report in this prospectus and will not be able to obtain Arthur Andersen's consent in the future. The absence of this consent may limit any recovery to which you might be entitled against Arthur Andersen under Section 11 of the Securities Act.

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.

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.

Investors in this offering will pay a much higher price than the book value of our common stock.

If you purchase common stock in this offering, you will pay more for your shares than the amounts paid by existing stockholders for their shares. As a result, you will incur immediate and substantial dilution of $9.53 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the initial public offering price of $14.00. In the past, we issued options and warrants to acquire common stock at prices significantly below the initial public offering price. To the extent these outstanding options or warrants are ultimately exercised, you will incur further dilution.

FORWARD-LOOKING INFORMATION

This prospectus contains forward-looking statements. The forward-looking statements are principally contained in the sections entitled "Prospectus Summary," "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited 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.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential" and similar expression intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk Factors." Also, these forward-looking statements represent our estimates and assumptions only as of the date of this prospectus.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is part, completely and with the understanding that our actual future results may be materially different from what we expect. You should assume that the information appearing in this prospectus is accurate as of the date on the front cover of this prospectus only. Our business, financial condition, results of operations and prospects may change. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the Federal securities laws to update and disclose material developments related to previously disclosed information. We qualify all of the information presented in this prospectus, and particularly our forward-looking statements, by these cautionary statements.

USE OF PROCEEDS

We estimate that the net proceeds we will receive from the sale of 3,750,000 shares of our common stock in this offering will be approximately $47.3 million, or approximately $54.6 million if the underwriters fully exercise their over-allotment option, in each case at the initial public offering price of $14.00 per share after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We anticipate using the net proceeds from this 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 plan to invest the net proceeds of the offering in short-term, interest bearing investment grade securities. After completion of the offering made by this prospectus, we anticipate that our annual research and development expense will increase to approximately $25 million to $30 million, with the majority of these costs incurred in connection with our Phase III clinical program for AI-700.

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 will retain broad discretion in the allocation and use of the net proceeds of this offering.

DIVIDEND POLICY

We have never declared or paid cash dividends on any class of our capital stock and do not anticipate paying any cash dividends on our common stock in the foreseeable future. We presently intend to retain future earnings, if any, to finance the expansion and growth of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors the board of directors deems relevant. In addition, the terms of any future debt or credit facility may preclude us from paying these dividends.

CAPITALIZATION

The following table describes our capitalization as of June 30, 2003:

- on an actual basis;
- on an as adjusted basis to give effect to (a) the conversion on July 1, 2003 of 3,731,999 shares of our preferred stock into 732,600 shares of our common stock in connection with the issuance of our 10% convertible promissory notes, (b) the conversion of all of our remaining outstanding convertible preferred stock and our outstanding 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, into 8,527,165 shares of our common stock upon the closing of this offering, (c) the amendment of our certificate of incorporation on September 12, 2003 in order to, among other things, increase the number of authorized shares of common stock, and (d) the sale of 3,750,000 shares of common stock by us in this offering at the initial offering price of $14.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of June 30, 2003	
	Actual	As Adjusted
	(in thousands, except share data)	
Convertible notes	$ 18,843	$ —
Long-term debt, net of current portion	644	644
Convertible preferred stock; $0.01 par value per share; 32,106,077 shares authorized, 31,145,083 shares issued and outstanding, actual; no shares authorized, issued and outstanding, as adjusted	94,702	—
Stockholders' (deficit) equity:		
Undesignated preferred stock; $0.01 par value per share; no shares authorized, issued and outstanding, actual; 5,000,000 shares authorized, no shares issued and outstanding, as adjusted		
Common stock; $0.01 par value per share; 11,741,127 shares authorized, 1,234,679 shares issued actual; 98,500,000 shares authorized, 14,244,444 shares issued, as adjusted	12	142
Additional paid-in capital	36,085	198,204
Treasury stock, 6,027 shares, at cost	(1)	(1)
Deferred stock-based compensation	(2,373)	(2,373)
Deficit accumulated during the development stage	(130,737)	(131,692)
Total stockholders' (deficit) equity	(97,014)	64,280
Total capitalization	$ 17,175	$ 64,924

The above table excludes:

- 914,976 shares of common stock issuable upon exercise of stock options outstanding as of June 30, 2003 at a weighted average exercise price of $2.63 per share;
- 581,825 shares of common stock issuable upon exercise of warrants outstanding as of June 30, 2003 at a weighted average exercise price of $10.64 per share;
- 89,605 shares of common stock issuable upon exercise of a purchase option outstanding as of June 30, 2003 at an exercise price of $16.74 per share, which purchase option will expire upon completion of the offering made by this prospectus; and
- shares subject to the underwriters' over-allotment option.

DILUTION

Our pro forma net tangible book value as of June 30, 2003 was approximately $16.3 million, or $1.55 per share of common stock. Pro forma net tangible book value per share represents the amount of our pro forma total tangible assets less total liabilities, divided by the pro forma number of shares of common stock outstanding, after giving effect to the conversion of all of our outstanding convertible preferred stock and our outstanding 10% convertible promissory notes, including interest accrued through September 5, 2003. After giving effect to the issuance and sale by us of the shares of common stock offered by this prospectus and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of June 30, 2003 would have been $63.7 million, or $4.47 per share. This represents an immediate increase in the pro forma net tangible book value of $2.92 per share to existing stockholders and immediate dilution of $9.53 per share to new stockholders participating in this offering. This dilution is illustrated by the following table:

Initial public offering price per share		$14.00
Pro forma net tangible book value per share before this offering	$1.55	
Increase per share attributable to this offering	2.92	
Pro forma net tangible book value per share after the offering		4.47
Dilution per share to new investors		$ 9.53

Assuming the exercise in full of the underwriters' over-allotment option, our pro forma net tangible book value as of June 30, 2003 would have been $71.0 million, or $4.80 per share. This represents an immediate increase in the pro forma net tangible book value of $3.25 per share to existing stockholders and an immediate decrease in net tangible book value of $9.20 per share to new investors.

The following table sets forth, on a pro forma basis as of June 30, 2003, the number of shares of common stock purchased from us, after giving effect to the conversion of all of our outstanding convertible preferred stock and our outstanding 10% convertible promissory notes, including interest accrued through September 5, 2003, the total consideration paid to us and the average price per share paid and to be paid by existing and new stockholders at the initial public offering price of $14.00 per share before deducting underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration		
	Number	Percent	Amount	Percent	Per Share
Existing stockholders	10,488,416	74%	$117,058,431	69%	$11.16
New stockholders	3,750,000	26	52,500,000	31	14.00
Totals	14,238,416	100%	$169,558,431	100%	

The foregoing discussion and tables assume no exercise of any stock options or warrants and no issuance of shares reserved for future issuance under our equity plans. The 10,488,416 shares purchased by existing stockholders excludes 6,027 shares in treasury stock. As of June 30, 2003, there were options outstanding to purchase 914,976 shares of our common stock at a weighted average exercise price of $2.63 per share and warrants outstanding to purchase 581,825 shares of our common stock at a weighted average exercise price of $10.64 per share. Also, as of June 30, 2003, an option to purchase 89,605 shares of our common stock at an exercise price of $16.74 per share was outstanding, which option will expire upon completion of the offering made by this prospectus. To the extent that any of these options or warrants are exercised, your investment will be further diluted. In addition, we may grant more options or warrants in the future.

SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with, and are qualified by reference to, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this prospectus. The statement of operations data for the years ended December 31, 2000, 2001 and 2002 and the balance sheet data as of December 31, 2001 and 2002 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The statement of operations data for the years ended 1998 and 1999 and the balance sheet data as of December 31, 1998, 1999 and 2000 are derived from our audited consolidated financial statements not included in this prospectus. The selected consolidated financial data as of June 30, 2003 and for the six months ended June 30, 2002 and 2003, as revised, have been derived from our unaudited financial statements included elsewhere in this prospectus. In the opinion of management, these unaudited financial statements have been prepared on a basis consistent with the audited financial statements and include all adjustments, consisting of normal and recurring adjustments, necessary for a fair presentation of the results for these periods and as of such date. The selected consolidated financial data set forth below for the six months ended June 30, 2003 are not necessarily indicative of our future results of operations or financial performance.

	Year Ended December 31,					Six Months Ended June 30,	
	1998	1999	2000	2001	2002	2002	2003
	(in thousands, except per share data)						
Statement of Operations Data:							
Operating expenses:							
Research and development	$ 8,190	$ 7,022	$ 9,978	$ 11,536	$ 13,545	$ 7,426	$ 6,248
General and administrative	1,429	1,622	2,517	3,893	3,906	1,825	1,855
Stock-based compensation	—	5	16	1,076	2,195	1,122	712
Total operating expenses	9,619	8,649	12,511	16,505	19,646	10,373	8,815
Equity in loss of joint venture	—	—	(12,015)	(1,965)	(1,183)	(808)	—
Interest and other income (expense), net	204	(492)	97	193	(1,067)	(593)	(1,092)
Net loss	(9,415)	(9,141)	(24,429)	(18,277)	(21,896)	(11,774)	(9,907)
Accretion of dividends and offering costs on preferred stock	(2,411)	(2,604)	(4,218)	(6,249)	(6,666)	(3,284)	(3,235)
Net loss available to common stockholders	$(11,826)	$(11,745)	$(28,647)	$(24,526)	$(28,562)	$(15,058)	$(13,142)
Basic and diluted net loss per common share	$ (28.32)	$ (27.24)	$ (64.20)	$ (50.82)	$ (35.40)	$ (30.24)	$ (10.87)
Basic and diluted weighted average common shares outstanding	418	432	446	483	807	498	1,209

	As of December 31,					As of June 30,
	1998	1999	2000	2001	2002	2003
	(in thousands)					
Balance Sheet Data:						
Cash, cash equivalents and short-term investments	$ 11,623	$ 2,230	$ 25,275	$ 15,599	$ 7,992	$ 15,624
Working capital	9,480	(1,498)	18,457	10,749	2,899	(5,953)
Total assets	14,860	5,104	29,092	24,457	13,367	20,405
Long-term debt, net of current portion	6,148	4,288	1,104	5,290	1,726	644
Redeemable convertible preferred stock	29,936	32,540	85,009	97,739	91,467	94,702
Total stockholders' deficit	(23,742)	(35,482)	(64,030)	(86,228)	(85,348)	(97,014)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion in conjunction with our consolidated financial statements, the related notes and other financial information appearing elsewhere in this prospectus.

Overview

We were incorporated in July 1993 as Polymers for Medicine, Inc. In March 1994, we changed our name to Acusphere, Inc. Since our inception, we have been a specialty pharmaceutical company engaged in the development of new drugs and improved formulations of existing drugs using our proprietary porous microparticle technology. Our company was founded based on insights by Dr. Robert Langer, the Kenneth Germeshausen Professor of Chemical and Biomedical Engineering at the Massachusetts Institute of Technology.

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 placement of equity securities, equipment leases and debt financings. We have not been profitable and have incurred a cumulative net loss of $103.2 million from inception through June 30, 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 begin operating as a 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 June 30, 2003, we cumulatively spent $64.6 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 June 30, 2003, we have cumulatively incurred $17.8 million in general and administrative expense.

Stock-Based Compensation Expense. Stock-based compensation expense, which is a non-cash charge, results 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. 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 June 30, 2003, we deferred $2.4 million in stock-based compensation and, from inception through June 30, 2003, recognized stock-based compensation expense of $4.1 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 will occur upon the completion of the offering made by this prospectus, our convertible preferred stock is entitled to accretion of dividends, the amount of which decreases the amount of stockholders' equity available to common stockholders and effectively increases the loss per share of common stock. Upon completion of the offering made by this prospectus, no convertible preferred stock will be outstanding, and accordingly there will be no further accretion of dividends and offering costs on these shares.

Six Months Ended June 30, 2002 and 2003

Research and Development Expense. Research and development expense decreased $1.2 million, or 16%, to $6.2 million in the six months ended June 30, 2003 from $7.4 million in the six months ended June 30, 2002. Research and development expense was higher in the six months ended June 30, 2002 as compared to the six months ended June 30, 2003 primarily due to one-time startup costs, including manufacturing of clinical materials, database development costs and clinical site training costs, incurred in connection with the commencement in 2002 of our Phase I clinical trial of AI-850. Lower research and development expense in the six months ended June 30, 2003 was partially offset by $632,000 in increased costs incurred in 2003 in connection with the commencement of our AI-700 Phase III clinical program.

The following table summarizes the primary components of our research and development expense for the six months ended June 30, 2003 and 2002. 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.

	Six Months Ended June 30,	
	2002	2003
	(in thousands)	
AI-700	$3,193	$3,306
AI-850 and AI-128	1,617	459
Other	683	595
Total direct costs	5,493	4,360
Facility costs	1,113	971
Depreciation	705	805
Patent costs	115	112
Total research and development expense	$7,426	$6,248

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 the six months ended June 30, 2003 of $3.3 million compared to $3.2 million in the six months ended June 30, 2002. Of these amounts, $494,000 for the six months ended June 30, 2003 and $1.3 million for the six months ended June 30, 2002 were incurred in connection with the production of clinical trial material by a third-party contract manufacturer, Hollister-Stier Laboratories LLC. In the six months ended June 30, 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 2003. 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 2003 and 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. Although we currently plan to file an NDA for AI-700 before the end of 2005, we cannot assure you that we will complete our Phase III clinical trial on this schedule, or at all.

- *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 the six months ended June 30, 2003 of $459,000 compared to $1.6 million in the six months ended June 30, 2002. Of these amounts, $531,000 for the six months ended June 30, 2002 was incurred in connection with the production of clinical trial material by a third-party contract manufacturer, Hollister-Stier Laboratories. There were no contract manufacturing costs incurred in connection with these product development programs during the six months ended June 30, 2003. These amounts exclude direct costs of $731,000 incurred in the six months ended June 30, 2002 for pulmonary drug development through the Elan joint venture, which was terminated in September 2002. We anticipate that our overall costs for development of these product candidates will decline until we are prepared to commence further pre-clinical and clinical testing using our own resources or through strategic collaborations. Although we expect to complete our Phase I dose escalation

study for AI-850 in 2004, we cannot assure you that we will complete our Phase I study on this schedule, or at all. We completed our initial Phase I study for AI-128 in 2002.

- *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 are subject to risks and uncertainties, including the requirement to seek regulatory approval, that 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.

These risks and uncertainties also prevent us from estimating with any certainty the specific timing and future costs of our clinical development programs, although historical trends at similarly situated companies indicate that expenses tend to increase in later stages of development. However, after completion of the offering made by this prospectus, we anticipate that our annual research and development expense will increase to approximately $25 to $30 million, with the majority of these costs incurred in connection with our Phase III clinical program for AI-700. The level to which our overall research and development costs increase in the near term will principally depend upon the rate at which clinical sites enroll patients for our AI-700 Phase III clinical program.

General and Administrative Expense. General and administrative expense totaled $1.8 million in each of the six months ended June 30, 2003 and June 30, 2002. The higher general and administrative expense of $30,000 incurred in the six months ended June 30, 2003 included increased depreciation expense of $86,000 and increased personnel costs of $69,000 partially offset by decreased legal costs of $63,000 and $59,000 of costs incurred in 2002 in connection with the move to our current facility. After the completion of the offering made by this prospectus, we anticipate incurring increases in general and administrative expense, such as increased 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 increased internal and external business development costs to support our various product development efforts, which can vary from period to period. Until we complete enrollment of a significant portion of the patients required in the AI-700 Phase III clinical program, we do not anticipate incurring significantly increased costs to accelerate preparations for commercial introduction of AI-700.

Stock-Based Compensation Expense. After giving effect to the additional $269,000 of compensation expense as discussed in note 12 to the consolidated financial statements, stock-based compensation expense decreased $410,000, or 37%, to $712,000 in the six months ended June 30, 2003 from $1.1 million in the six months ended June 30, 2002. Stock-based compensation expense incurred in the six months ended June 30, 2003 resulted from the vesting of stock options granted in prior periods on which deferred compensation had previously been recorded and on stock options granted during the six months ended June 30, 2003.

Equity in Loss of Joint Venture. Our joint venture with Elan was terminated in September 2002. During the six months ended June 30, 2002, we recognized a $808,000 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. 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) increased $499,000, or 84%, to a net expense of $1.1 million in the six months ended June 30, 2003 from a net expense of $593,000 in the six months ended June 30, 2002. During these periods, interest and other income (expense) consisted of the following:

	Six Months Ended June 30,	
	2002	2003
Interest income	$ 116,000	$ 69,000
Other income (expense)	9,000	(121,000)
Interest expense	(718,000)	(1,040,000)
Total, net	$(593,000)	$(1,092,000)

The decrease in interest income in the six months ended June 30, 2003 compared to the six months ended June 30, 2002 was primarily due to reduced yields on investments resulting from lower average interest rates and to lower average fund balances available for investment. The increase in interest expense in the six months ended June 30, 2003 compared to the six months ended June 30, 2002 was primarily due to $121,000 of costs incurred in connection with early repayment of debt, and $164,000 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.

Accretion of Dividends and Offering Costs on Convertible Preferred Stock. Accretion of dividends and offering costs on convertible preferred stock totaled $3.2 million in each of the six months ended June 30, 2003 and June 30, 2002. In the six months ended June 30, 2003, a decrease of $128,000 from dividends on convertible preferred stock was partially offset by an increase of $79,000 from the accretion of Series J convertible preferred stock offering costs. The decrease in dividends primarily resulted from the conversion of certain shares of convertible preferred stock to common stock in connection with our Series J convertible preferred stock financing. Upon completion of the offering made by this prospectus, no convertible preferred stock will be outstanding, and accordingly there will be no further accretion of dividends and offering costs on these shares.

Years Ended December 31, 2000, 2001 and 2002

Research and Development Expense. Research and development expense for the year ended December 31, 2002 was $13.5 million, compared to $11.5 million in 2001 and $10.0 million in 2000. The $2.0 million increase in 2002 over 2001 represented an increase of 17% and the $1.5 million increase in 2001 over 2000 represented an increase of 16%.

In 2002 compared to 2001, our increased research and development expense principally resulted from increased facility costs and increased pulmonary drug development costs, net of costs attributable to the Elan joint venture. In 2001 compared to 2000, the higher level of research and development expense was primarily associated with acceleration of our AI-850 research and development efforts.

The following table summarizes the primary components of our research and development expense for the years ended December 31, 2002, 2001 and 2000. 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,		
	2000	2001	2002
		(in thousands)	
AI-700	$5,758	$ 5,209	$ 5,332
AI-850 and AI-128	1,787	3,481	2,992
Other	656	98	1,490
Total direct costs	8,201	8,788	9,814
Facility costs	565	1,093	2,106
Depreciation	982	1,280	1,363
Patent costs	230	375	262
Total research and development expense	$9,978	$11,536	$13,545

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 2002 of $5.3 million, in 2001 of $5.2 million and in 2000 of $5.8 million. Of these amounts, $1.6 million in 2002 and $1.4 million in 2001 was incurred in connection with the production of clinical trial material by a third-party contract manufacturer, Hollister-Stier Laboratories. There were no contract manufacturing costs incurred in connection with this product development program in 2000. We anticipate that the new clinical sites for this clinical program, in both Europe and North America, will be trained and initiated during 2003. We believe that our research and development expenses for the AI-700 Phase III program will increase as new clinical sites join in the Phase III clinical program and as the number of patients enrolled in our Phase III program increases. As clinical sites are initiated and patients are enrolled in the Phase III clinical program, we anticipate incurring increased costs from professional service firms helping to support the clinical trial in clinical trial matters 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 2003 and 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. Although we currently plan to file an NDA for AI-700 before the end of 2005, we cannot assure you that we will complete our Phase III clinical trial on this schedule, or at all.

- *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 2002 of $3.0 million, in 2001 of $3.5 million and in 2000 of $1.8 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, Hollister-Stier Laboratories. There were no contract manufacturing costs incurred in connection with these product development programs in 2000. 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 our overall costs for development of these product candidates will decline until we are prepared to commence further pre-clinical and clinical testing using our own resources or through strategic collaboration. Although we expect to complete our Phase I dose escalation study for AI-850 in 2004, we cannot assure you that we will complete our Phase I study on this schedule, or at all. We completed our initial Phase I study for AI-128 in 2002.

- *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 are subject to risks and uncertainties, including the requirements to seek regulatory approval, that 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 reasonably predict 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.

These risks and uncertainties also prevent us from estimating with any certainty the specific timing and future costs of our clinical development programs, although historical trends indicate that expenses tend to increase in later stages of development. However, after completion of the offering made by this prospectus, we anticipate that our annual research and development expense will increase to approximately $25 to $30 million, with the majority of these costs incurred in connection with our Phase III clinical program for AI-700. The level to which our overall AI-700 research and development costs increase in the near term will principally depend upon the rate at which clinical sites enroll patients.

General and Administrative Expense. General and administrative expense for each of the years ended December 31, 2002 and December 31, 2001 was $3.9 million. General and administrative expense for the year ended December 21, 2000 was $2.5 million. The increase in 2001 over 2000 represented an increase of 55%.

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.

In 2001 compared to 2000, the increase in general and administrative expense included $682,000 in increased legal, accounting and printing costs, which costs were primarily attributable to our financing activities in 2001. On September 4, 2001, we filed a registration statement with the SEC seeking to commence an initial public offering of our common stock. On December 5, 2001, we withdrew our registration statement without incurring any roadshow costs. In addition to the increase in legal, accounting and printing fees in 2001 compared to 2000, we incurred approximately $324,000 in increased salary and temporary labor costs, primarily from the hiring of additional personnel, including senior level management. We also incurred increased costs in 2001 compared to 2000 for facilities, depreciation, consulting and travel.

Stock-Based Compensation Expense. Stock-based compensation expense for the year ended December 31, 2002 was $2.2 million, compared to $1.1 million in 2001 and $16,000 in 2000. In connection with the grant of stock options to employees and non-employees, we recorded deferred compensation of $5.0 million in 2001 and $162,000 in 2000 which is being recognized as additional expense over the remaining vesting life of these options. In addition, in connection with the grants of restricted stock to directors and advisors, we recorded deferred compensation of $344,000 in 2001 which is being recognized

as additional expense over the remaining vesting life of these options. These deferred amounts are subject to adjustment for forfeiture over their respective vesting periods. No deferred compensation was recorded in 2002 in connection with stock options granted in 2002.

Equity in Loss of Joint Venture. Our portion of the loss from the Elan joint venture was $1.2 million in 2002, $2.0 million in 2001 and $12.0 million in 2000. Our joint venture with Elan was terminated in September 2002 after which all costs relating to the development of pulmonary drug delivery candidates were consolidated as part of research and development expense. We anticipate that in the near term, our research and development expenses for pulmonary drug delivery candidates will be incurred at a lower rate than what was being incurred as our equity in loss from the joint venture. During 2000, equity in loss of joint venture included our portion of the joint venture's one-time purchase of an exclusive license to certain aspects of Elan's drug delivery technology amounting to $12.0 million.

Interest and Other Income (Expense). Interest and other income (expense) decreased to a net expense of $1.1 million in 2002 from $193,000 in net income in 2001 after having increased from net income of $97,000 in 2000. During these years, interest and other income (expense) consisted of the following:

	Years Ended December 31,		
	2000	2001	2002
Interest income	$ 912,000	$ 943,000	$ 224,000
Other income	—	—	9,000
Interest expense	(815,000)	(750,000)	(1,300,000)
Total, net	$ 97,000	$ 193,000	$(1,067,000)

The decrease in interest income in 2002 compared to 2001 was primarily due to reduced yields on investments resulting from lower average interest rates and to lower average fund balances 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 notes payable. As of December 31, 2002, the unamortized value of the warrants was $177,000.

Accretion of Dividends and Offering Costs on Convertible Preferred Stock. Accretion of dividends and offering costs on convertible preferred stock was $6.7 million in 2002, $6.2 million in 2001 and $4.2 million in 2000. These increases reflect the 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. Upon completion of the offering made by this prospectus, no convertible preferred stock will be outstanding, and accordingly there will be no further accretion of dividends and offering costs on these shares.

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 June 30, 2003, we had cash, cash equivalents and short-term investments of $15.6 million. Since our inception in July 1993 through June 30, 2003, we have raised $94.5 million through the issuance of equity securities. As of June 30, 2003 we owed $19.4 million from convertible promissory notes and $1.5 million from capital leases and had commitments totaling $20.4 million for rent under our facility lease.

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 the offering made by this prospectus, the 10% convertible promissory notes and interest accrued thereon will convert into common stock at $8.46 per share, which is the price of the Series J convertible preferred stock issued in June and July 2002, our last round of private equity financing.

During the six months ended June 30, 2003, operating activities used $7.4 million of cash. Net cash used by operating activities during this period resulted primarily from a net loss of $9.9 million. This use of cash was partially offset by increases in accrued expenses of $302,000, increases in accounts payable of $97,000, increases in prepaid assets and other assets of $67,000 and non-cash charges for depreciation and amortization of $1.1 million and non-cash charges for stock-based compensation expense of $712,000 and non-cash interest expense of $337,000.

During the year ended December 31, 2002, operating activities used $17.7 million of cash. Net cash used by operating activities during this period resulted primarily from a net loss of $21.9 million, a decrease in accounts payable of $718,000 and a decrease of $778,000 in amounts due from the Elan joint venture. These uses of cash were partially offset by increases in accrued expenses of $142,000, and, decreases in other current assets of $5,000 and non-cash charges for stock-based compensation expense, depreciation and amortization, non-cash interest expense and non-cash rent of $2.2 million, $1.7 million, $384,000 and $54,000, respectively.

During the six months ended June 30, 2003, investing activities used $4.0 million in cash. Purchases of short term investments used $3.5 million, $253,000 for purchases of equipment and an increase in other assets of $243,000.

During the year ended December 31, 2002, investing activities provided $8.4 million in cash. During 2002, $9.1 million in cash provided from the maturity of short-term investments was partially offset by $687,000 for purchases of equipment and an increase in other assets of $34,000.

During the six months ended June 30, 2003, financing activities provided $15.5 million in cash, with proceeds of $19.4 million from the issuance of 10% convertible promissory notes which were partially offset by $4.0 million for scheduled and early repayment of debt.

During the year ended December 31, 2002, financing activities provided $10.8 million in cash. During 2002, net proceeds from the sale of Series J convertible preferred stock provided $14.3 million in cash which was partially offset by $3.5 million in cash used for the scheduled repayment of debt.

The following table summarizes our contractual obligations at June 30, 2003 and the effects such obligations are expected to have on our liquidity and cash flows in future periods.

Payments Due by Period

Contractual Obligations	Total	July - December 2003	2004 Through 2005	2006 Through 2007	After 2007
			(in thousands)		
Capital lease obligations	$ 1,518	$ 428	$1,090	$ —	$ —
Operating lease obligations	20,377	1,033	4,349	4,658	10,337
Total contractual cash obligations	$21,895	$1,461	$5,439	$4,658	$10,337

Excluded from the above table of commitments at June 30, 2003 is $19.4 in 10% convertible promissory notes due June 30, 2004 issued by us during April and June 2003. These notes and interest accrued thereon will convert into common stock upon completion of the offering made by this prospectus.

Based on our operating plans, we believe that the proceeds from this offering, 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 twelve months from the date of this prospectus. 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

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.

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 its 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 have not been publicly traded, 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.

As disclosed more fully in Note 7 to our consolidated financial statements, in lieu of cash payments we granted the following numbers of shares of restricted common stock and options to purchase common stock to non-employees during the years ended December 31, 2002, 2001 and 2000:

Year Ending December 31,	Exercise Price Per Share	Number of Shares	Number of Options
2002	-	—	—
2001	$0.06 - $7.20	13,791	—
2000	1.98 - 5.70	3,036	10,000

In addition, we granted 14,956 shares of restricted common stock at a price of $0.06 per share during the six months ended June 30, 2003. We recorded these grants at fair value when granted. Because certain of these awards vest or can be repurchased over time, we recorded $102,000 in the six months ended June 30, 2003 and $464,000 in 2001 and $54,000 in 2000, of the value of these grants as deferred stock-based compensation. This included deferred compensation for non-qualified option grants to non-employees. We amortize the deferred amounts as charges to operations over the vesting periods of the grants or repurchase options. This resulted in deferred stock-based compensation expense of $110,000 in the six months ended June 30, 2003, $27,000 in 2002, $146,000 in 2001 and $11,000 in 2000. The fair value of the unvested portion of these grants is periodically remeasured resulting in charges or credits to operations in periods when such remeasurement results in differences between the fair value of the underlying common stock and the exercise price of the options that is greater than or less than the differences, if any, between the fair value of the underlying common stock and the exercise price of the options at their respective previous measurement dates.

As disclosed more fully in Note 7 to our consolidated financial statements, we granted the following number of stock options to employees during the years ended December 31, 2002, 2001 and 2000:

Year Ending December 31,	Exercise Price Per Share	Number of Shares
2002	$0.84 - $7.20	366,429
2001	5.70 - 7.20	230,119
2000	1.98 - 5.70	71,101

In addition, we granted options to purchase 197,726 shares of our common stock to employees during the six months ended June 30, 2003 at a price of $0.84 per share. Included in the options granted during these periods were options deemed for accounting purposes to have been granted with exercise prices below their then current market value. We recorded the value of these differences, $1.4 million in the six months ended June 30, 2003, $4.9 million in 2001 and $112,000 in 2000, as deferred stock-based compensation. We amortize the deferred amounts as charges to operations over the vesting periods of the grants, resulting in deferred stock-based compensation expense relating to these options of $604,000 in the six months ended June 30, 2003, $2.2 million in 2002, $929,000 in 2001 and $5,000 in 2000. We anticipate recording stock-based compensation of $607,000 in the last six months of 2003, $789,000 in 2004, $484,000 in 2005 and $326,000 in 2006, less adjustment for forfeitures, relating to the amortization of deferred compensation recorded as of June 30, 2003.

During the six months ended June 30, 2003, we also granted warrants in connection with our issuance of $19.4 million in convertible promissory notes. After giving effect to the conversion of all of our outstanding shares of convertible preferred stock upon the closing of this offering, the warrants that we granted in connection with the issuance of these notes may be exercised to purchase 459,569 shares of common stock. The warrants are exercisable at a price of $8.46 per share. The value ascribed to the warrants and related discount recorded using the Black-Scholes pricing model totaled $761,000 and is being amortized to interest expense through the maturity date of the notes or June 30, 2004.

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 involved 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, 2002, we had federal tax net operating loss carryforwards of $55.8 million, which expire through 2022. We also have research and development credit carryforwards of $2.1 million. We have recorded a valuation allowance of $38.2 million as an 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 May 2003, the FASB issued SFAS No. 150, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*. This statement establishes how a company classifies and measures certain financial instruments with characteristics of both liabilities and equity, including redeemable preferred stock. This statement is effective for financial instruments entered into or modified after May 31, 2003, and otherwise effective at the beginning of the interim period commencing July 1, 2003, except for mandatorily redeemable financial instruments of nonpublic companies. We have not yet determined the impact of this statement on our financial statements.

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 June 30, 2003, we estimate that the fair value of our investment portfolio would decline by an immaterial amount. While our cash and investment balances will increase upon completion of the offering made by this prospectus, we will have the ability to hold our fixed

income investments until maturity, and therefore we would 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.

Change in Accountants

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 as presented in this prospectus 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 on any financial or accounting reporting matters in the period before its appointment.

BUSINESS

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 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 microparticles in a versatile manner, so that we can customize the microparticles 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.
- *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 microparticles in a versatile manner so that we can customize the microparticles to address the delivery needs of a variety of drugs. We are focused on creating porous microparticles that are smaller than red blood cells. 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 Phase III trials for AI-700 and submit a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, by the end of 2005.

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.

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 will 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.

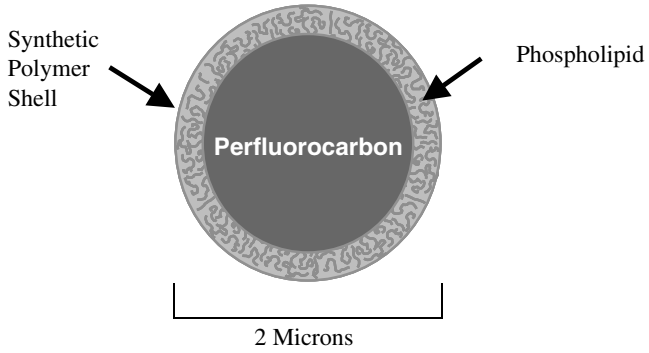
There is no ultrasound contrast agent approved by the FDA for use in stress echo or myocardial perfusion imaging. Ultrasound contrast agents have been approved by the FDA for left ventricular opacification, referred to as a resting wall motion study, which is a procedure for looking at the heart wall 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 filed these results and our protocol for our Phase III trials with the FDA in late 2001. We initiated our Phase III program in early 2003 and plan to file an NDA for AI-700 in 2005.

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. 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 of approximately 300 patients with suspected coronary artery disease per trial. The Phase III trials will take place at clinical sites in North America and Europe with data from the trials intended for submission to both U.S., Canadian and European regulatory authorities. The endpoints for the trial are sensitivity and specificity in comparison to nuclear stress, 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.

Our plan is to commence the pivotal phase of our Phase III AI-700 clinical trial before the end of 2003, complete initiating U.S. and European clinical trial sites in the pivotal trials in the first half of 2004, cumulatively enroll 300 patients in the Phase III program by the end of 2004 and complete patient enrollment in the pivotal trials and file for an NDA for AI-700 before the end of 2005. Although these milestones and target completion dates reflect our current plan, we cannot assure you that we will complete these milestones on this schedule, or at all.

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

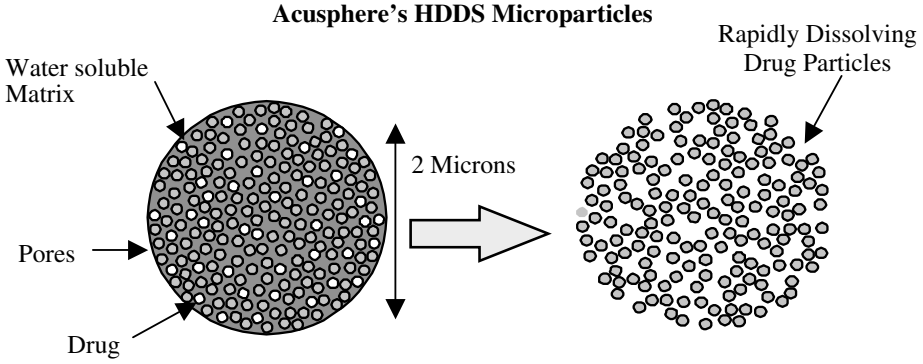
Broad Applications for the Delivery of Hydrophobic Drugs. We have developed a proprietary formulation technology called HDDS that converts drugs that do not dissolve well in water, or hydrophobic drugs, into small microparticles that rapidly dissolve in water. Formulation of hydrophobic drugs is often 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 a competitive disadvantage due to a less than ideal formulation. 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 $857 million in 2002, 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 slow 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 Microparticles. 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. HDDS technology uses a proprietary high efficiency spray drying process and pore forming agent technology to create wettable, sponge-like, microparticles of drug in a water soluble carrier matrix. The end results are rapidly dissolvable dry powder formulations that can be used in oral, inhaled or intravenous administration.

Acusphere's HDDS Microparticles



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.

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.* Our pre-clinical safety studies suggest that it takes eight times higher doses of AI-850 to cause similar adverse effects in rats as the doses of Taxol that causes mortality in some animals. As a result, we believe AI-850 has the potential to minimize or eliminate some of the side effects of Taxol.
- *Shorter Administration.* In our pre-clinical studies, we demonstrated that AI-850 can be administered by relatively quick injections. In our Phase I trial, we have been injecting AI-850 in humans using injections that are less than 30 minutes, which are more convenient and can be less expensive than a slow infusion because less nursing care is required. In comparison, Taxol must be slowly infused over a three-hour period.
- *Improved Efficacy at Higher Doses.* Our pre-clinical studies have demonstrated improved efficacy of high-dose AI-850 relative to the maximum tolerated dose of Taxol in a variety of tumor types. For instance, in pre-clinical studies in mice implanted with human breast cancer tumors, we administered doses of AI-850 that were approximately three times the maximum tolerated dose of Taxol. At these high doses, the tumors in mice treated with AI-850 shrank and remained below 100 milligrams in size, which is the level of detection of our assays, for more than 50% longer than the human breast cancer tumors implanted in mice treated with the maximum tolerated doses of Taxol.

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 early 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 and intravenously administered 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 improved formulations of approved asthma drugs that are off-patent. These approved asthma drugs each generated revenues in excess of $500 million in 2002.

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.

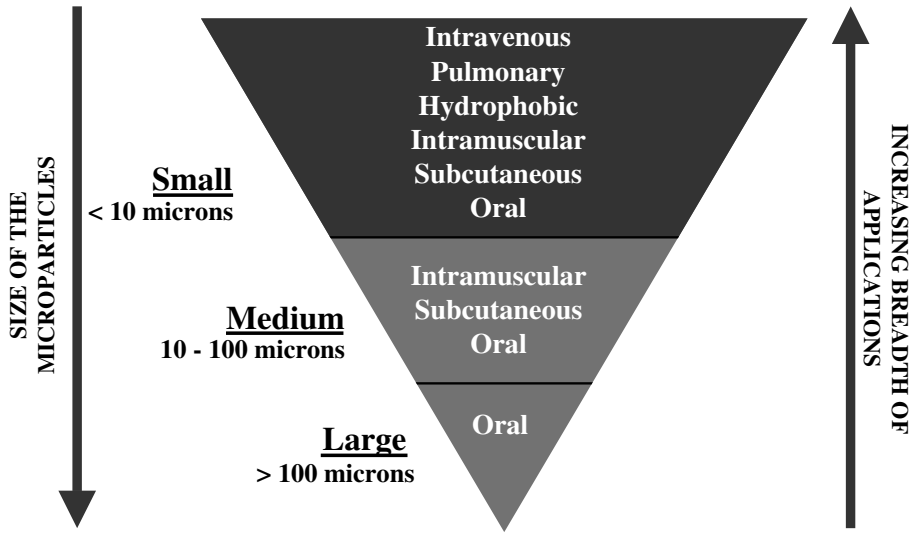
Clinical Results. We completed a European Phase I clinical trial with AI-128 in 2002. The study was conducted in accordance with applicable local regulatory requirements. In this trial, we demonstrated that approximately 80% of inhaled AI-128 was delivered to the intended target, the upper lung. These 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. In late 2002, we initiated pre-clinical studies of AI-495, a sustained release, dry-powder formulation of a widely-used drug to treat respiratory disease. We believe that such a formulation of this drug 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.

Small Microparticles Have Broad Applications



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 and throat for 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. These particles 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.

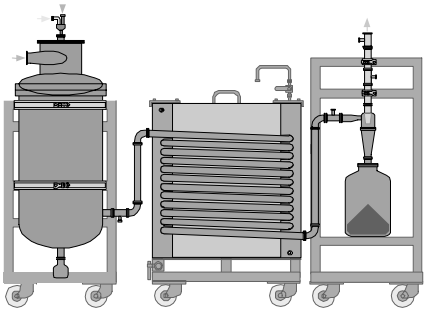
Our proprietary porous microparticle technology platform consists of two key components — a multi-chamber spray dryer and pore forming agents.

Our Patented Spray Dryers

We believe we have overcome the limitations of standard spray drying in producing small microparticles 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.



Primary Chamber **Secondary Chamber** **Collection Jar**

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 to be used in drugs delivered intravenously, the microparticles 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. We currently plan to manufacture commercial products 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.

We currently own twelve issued U.S. patents, one allowed U.S. patent applications and twelve 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. One issued U.S. patent and eight U.S. patent applications are related to various aspects of our porous microparticle drug delivery technology. Three issued U.S. patents, one allowed U.S. patent application 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 prospectus, 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.
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

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 prospectus 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. Accordingly, 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 that is in Phase III clinical trials. 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 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 prospectus 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 and Protarga 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 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 October 1, 2003, we had 55 full-time employees, including 45 in research and development and 10 in general and administrative. Eleven 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.

Facilities

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 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.

Legal Proceedings

We are not a party to any material legal proceedings.

MANAGEMENT

Executive Officers, Key Employees and Directors

The following table shows information about our executive officers, key employees and directors as of September 5, 2003.

Name	Age	Position
Sherri C. Oberg*	43	President, Chief Executive Officer and Director
Howard Bernstein, M.D., Ph.D.*	46	Senior Vice President, Research and Development
Charles P. Cox, Ph.D.*	51	Senior Vice President, Corporate Development and Marketing
Michael R. Slater*	56	Senior Vice President, Operations
John F. Thero*	42	Senior Vice President and Chief Financial Officer
Thomas M. Hanlon III	40	Vice President, Manufacturing and Materials Management
Richard Walovitch, Ph.D.	49	Vice President, Clinical Research
Frank Baldino, Jr., Ph.D.	50	Director
Martyn Greenacre	61	Director
Derek Lemke-von Ammon	45	Director
Terrance McGuire	47	Director
Kate Mitchell	44	Director

* Denotes executive officer.

Mr. McGuire, Ms. Mitchell and Dr. Baldino are members of our compensation committee. Mr. McGuire is chairperson of our compensation committee.

Dr. Baldino, Ms. Mitchell and Mr. Greenacre are members of our audit committee. Mr. Greenacre is chairperson of our audit committee.

Dr. Baldino and Mr. Greenacre are members of our nominating and corporate governance committee. Mr. Greenacre is chairperson of our nominating and corporate governance committee.

Sherri C. Oberg, a co-founder of Acusphere, has served as our President and Chief Executive Officer and one of our directors since our inception in 1993. Prior to joining Acusphere, Ms. Oberg was President and Chief Executive Officer of Neomorphics, Inc., a venture capital-backed company focused on tissue engineering, from 1991 to 1992. Prior to joining Neomorphics, she was a venture capitalist at Aegis Venture Funds from 1988 to 1991, and at Inco Venture Capital Management from 1986 to 1988. Ms. Oberg is a member of the Board of Overseers of The Amos Tuck School at Dartmouth College. Ms. Oberg holds a B.A. from Dartmouth College and an M.B.A. from the Amos Tuck School of Business Administration.

Howard Bernstein, M.D., Ph.D., has served as our Senior Vice President, Research and Development since January 2000 and as Vice President of Research and Development from 1994 to January 2000. Prior to joining Acusphere, Dr. Bernstein served as Vice President of Pharmaceutical Development at Alkermes, Inc. from 1992 to 1994 and as Vice President of Research at Enzytech Inc. from 1991 to 1992. Dr. Bernstein holds an M.D. from Harvard Medical School and a Ph.D. in Chemical Engineering from the Massachusetts Institute of Technology.

Charles P. Cox, Ph.D., has served as our Senior Vice President, Corporate Development and Marketing since August 2003. Prior to joining Acusphere, Dr. Cox was employed by Atrix Laboratories as Senior Vice President of Corporate Development from April 2001 to August 2003; as Vice President, New Business Development from January 1996 to April 2001; and as Vice President, Product Development from September 1992 to January 1996. He was employed by G.D. Searle & Co., Searle R&D Division from 1988 to 1992 as Project Director, R&D Planning and Management and as a Research Scientist, Molecular and Cellular Biology from 1985 to 1988. Dr. Cox holds an M.S. and Ph.D. in Medical

Microbiology and Immunology from the University of Oklahoma Health Sciences Center and an MBA from the J.L. Kellogg Graduate School of Management at Northwestern University.

Michael R. Slater, has served as our Senior Vice President, Operations since October 2001. Prior to joining Acusphere, Mr. Slater served as Vice President of Operations from April 1999 to June 2001, and as Vice President of Quality Systems and Regulatory Affairs from February 1998 to April 1999 at Anika Therapeutics, Inc. Mr. Slater served as an independent consultant to the biopharmaceutical industry from 1996 to 1998, as Executive Vice President, Development Operations for ImmuLogic Pharmaceutical Corporation from 1995 to 1996, as Vice President of Regulatory Affairs at Biogen, Inc. from 1985 to 1995, as Director of Corporate Regulatory Affairs from 1983 to 1985 at Biogen S.A. and in various positions including Senior Manager, Medical Services from 1971 to 1983 at Hoechst Pharmaceuticals. Mr. Slater holds a B.Sc. in Information Science from the Metropolitan University of Leeds, England.

John F. Thero, has served as our Senior Vice President, Finance and Administration, Treasurer and Chief Financial Officer since February 2003. Prior to joining Acusphere, Mr. Thero served at Abiomed, Inc. from 1994 to January 2003 as Senior Vice President Finance, Treasurer and Chief Financial Officer. From 1992 to 1994, he was Chief Financial Officer and acting President for the restructuring of two venture-backed companies. From 1987 to 1992 he was employed in various capacities including Chief Financial Officer by Aries Technology, Inc. From 1983 to 1987 he was employed by the commercial audit division of Arthur Andersen LLP, during which time he became a Certified Public Accountant. Mr. Thero received a B.A. in Economics/Accounting from The College of the Holy Cross.

Thomas M. Hanlon III, has served as Vice President, Manufacturing and Materials Management since January 2002; as Senior Director, Manufacturing and Process Development from January 1999 to December 2001; as Director of Manufacturing and Process Development from 1997 to January 1999; and as Associate Director, Manufacturing from 1996 to 1997. Prior to joining Acusphere, he served as Manager, Parenteral Manufacturing at Sandoz Pharmaceuticals, Inc. from 1992 to 1996 and as Supervisor, Solid Dosage Forms from 1987 to 1992 at Sandoz Pharmaceuticals, Inc. and as Supervisor, Solids at Ayerst Laboratories, a division of American Home Products, from 1985 to 1987. Mr. Hanlon holds a B.S. in Biology from Villanova University and an M.B.A. from the W. Paul Stillman School of Business, Seton Hall University.

Richard Walovitch, Ph.D., has served as our Vice President, Clinical Research since March 1997. Prior to joining Acusphere, Dr. Walovitch was Vice President of Pre-clinical and Clinical Research at Epix Medical Inc. (formerly Metasyn) from 1993 to 1997 and the International Project Clinician at DuPont Merck Pharmaceutical Company from 1988 to 1993. Dr. Walovitch holds a B.S. in Biology and a Ph.D. in Pharmacology from the University of Illinois.

Frank Baldino, Jr., Ph.D., has served as one of our directors since April 2001. Dr. Baldino is the founder of Cephalon, Inc., an integrated specialty biopharmaceutical company involved in the development of therapeutics for neurological disorders, sleep disorders and cancer. He has served as President, Chief Executive Officer and a Director of Cephalon since its inception in 1987 and is currently Chairman of the Board as well. Dr. Baldino holds adjunct academic appointments, including Adjunct Associate Professor of Pharmacology at Temple University School of Medicine, and Adjunct Associate Professor of Physiology and Biophysics and Adjunct Associate Professor of Neurology at Hahnemann University. Dr. Baldino is also a director of Pharmacopeia, Inc. and ViroPharma, Incorporated.

Martyn Greenacre, has served as one of our directors since July 2001. Mr. Greenacre served in various senior management positions at SmithKline Beecham from 1973 through 1992. From 1989 to 1992, as Chairman Europe, he was responsible for the strategic direction and operational management of pharmaceutical subsidiaries in Europe and for planning and executing European aspects of the merger between SmithKline Beckman and Beecham Pharmaceuticals. He has also served as Chief Executive Officer of two life sciences companies, Zynaxis Inc. from 1993 to 1997 and Delsys Pharmaceutical Corp. from 1997 to 2001. He is also a director of Cephalon, Inc., Curis, Inc. and Immune Response Corp.

Derek Lemke-von Ammon, has served as one of our directors since September 2002. Mr. Lemke-von Ammon is a Managing Partner for Thomas Weisel Capital Partners and a Director of Private Equity for Thomas Weisel Partners, a founding member of that Firm and a member of the Firm's Executive Committee. Prior to joining Thomas Weisel Capital Partners in 1998, Mr. Lemke-von Ammon was a Senior Managing Director and Director of Private Equity at Montgomery Securities from 1989 to 1998. Prior to joining Montgomery Securities, Mr. Lemke-von Ammon was a Vice President at Dain Bosworth Incorporated where he was employed from 1985 to 1989. He also worked as a corporate and securities attorney from 1983 to 1985 for Bogle & Gates in Seattle.

Terrance McGuire, has served as one of our directors since 1994. Mr. McGuire is a founder of Polaris Venture Partners, where he has served as a Managing General Partner since March 1996. He has also served as a General Partner with Burr, Egan, Deleage & Co. since 1992. Mr. McGuire also serves as a director of the Massachusetts Biotechnology Council, deCODE Genetics, Inc., and MassMedic.

Kate Mitchell, has served as one of our directors since January 2000. Ms. Mitchell is the President and Managing Director of BA Ventures, where she has served since 1997. Prior to joining BA Ventures, she was Senior Vice President for Bank of America Corporation-Interactive Banking from 1994 to 1996. Ms. Mitchell also serves as a director at Songbird Medical, Inc., Manage.com, Wayport, Inc. and Tonic Software, Inc.

Co-Founder and Consultants

Co-Founder

Robert S. Langer, Sc.D., is the Kenneth Germeshausen Professor of Chemical and Biomedical Engineering at the Massachusetts Institute of Technology and a co-founder of Acusphere with Ms. Oberg. He is one of very few people ever elected to all three U.S. National Academies — the National Academy of Sciences, the Institute of Medicine and the National Academy of Engineering. He also served as Chairman of the Science Board at the FDA, from 1999-2002. In 1996, he received the Gairdner Foundation Award, one of the most prestigious awards in medical science. This award has only been in existence since 1957, and 54 of its recipients have subsequently won the Nobel Prize.

Business Development

We utilize consultants to advise us on aspects of our business, including business development, and for many years have worked closely with William I. Ramage, our Executive Consultant. Dr. Ramage currently is working with us on potential partnering and strategic marketing arrangements for our lead product candidate, AI-700.

William I. Ramage, D. Phil., has served as an Executive Consultant at Acusphere since March 2000 and as an Independent Business Development and Strategic Marketing Consultant to us from August 1999 until March 2000 and to other clients since November 1998. Prior to Acusphere, Dr. Ramage was Vice President Business Development and Marketing at Molecular BioSystems from September 1996 until November 1998, and Vice President Business Development and Customer Services at DuPont Merck, a leader in nuclear imaging agents for myocardial perfusion imaging, from April 1995 until September 1996. Dr. Ramage holds a B.Sc. from the University of Glasgow and a D.Phil. from Oxford University.

Scientific Advisors

We also utilize leading researchers and physicians to advise us on scientific, medical and technical matters related to our product candidates. Our scientific advisors advise our management on strategic issues related to our scientific development programs. In return for their services, these advisors may receive compensation in the form of cash and/or shares of or options to purchase shares of our common stock. Our scientific advisors are experts in fields such as materials science and encapsulation and cardiology.

Materials Sciences and Encapsulation

Edith Mathiowitz, Ph.D., is Associate Professor of Medical Science in the Section of Artificial Organs, Biomaterials, and Cellular Technology at Brown University. Dr. Mathiowitz has over twenty years of experience in the fields of microencapsulation, synthetic polymer engineering and drug delivery. She has published 67 papers and 25 patents in these areas. Her research interests include drug delivery and microencapsulation, gene therapy, cell encapsulation and biomaterials engineering.

Cardiology

Michael Picard, M.D., is Director of the Cardiac Ultrasound Laboratory at Massachusetts General Hospital and Associate Professor of Medicine at Harvard Medical School. Dr. Picard has extensive knowledge of the second generation ultrasound contrast agents. He has participated as an investigator in the clinical trials of Mallinkrodt, DuPont, Schering AG and Bracco, and has been a reader in the core echo lab of Alliance Pharmaceuticals, which developed Imagent. Dr. Picard also serves as our medical monitor for AI-700.

Natesa Pandian, M.D., is Director of Cardiovascular Imaging and Hemodynamic Laboratory at the New England Medical Center. Dr. Pandian is also an Associate Professor of Medicine and Radiology at Tufts University School of Medicine. Dr. Pandian is an internationally renowned expert in the field of ultrasound contrast agents and has extensive experience in the preclinical and clinical development of these agents.

Oncology

David Tuck, M.D., is an Associate Director of Yale Cancer Center. Dr. Tuck is also Assistant Professor, Department of Pathology, Yale University School of Medicine. Dr. Tuck also serves as our medical monitor for AI-850. Prior to joining Yale, Dr. Tuck was involved with the clinical development of Taxol at Bristol-Myers Squibb.

Board Composition

All of our current directors were selected as directors under a voting agreement that will automatically terminate upon the closing of this offering. Four of our current directors — Dr. Baldino, Messrs. Greenacre and McGuire and Ms. Mitchell — are independent directors as defined by the applicable rules of the National Association of Securities Dealers listing standards. We refer to these directors as our "independent directors." There are no family relationships among any of our directors or executive officers.

Following the closing of this offering, our board of directors will be divided into three classes, each of whose members will serve for a staggered three-year term. Our board of directors will consist of Mr. McGuire and Ms. Oberg as Class I directors, whose term of office will continue until the 2004 annual meeting of stockholders, Mr. Lemke-von Ammon and Ms. Mitchell as Class II directors, whose term of office will continue until the 2005 annual meeting of stockholders, and Dr. Baldino and Mr. Greenacre as Class III directors, whose term of office will continue until the 2006 annual meeting of stockholders. At each annual meeting of stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the total number of directors. This classification of the board of directors could have the effect of delaying or preventing changes in control or management of Acusphere. See "Description of Capital Stock — Anti-Takeover Effects of Provisions of Delaware Law and Our Certificate of Incorporation and By-Laws."

Committees of the Board of Directors

Our board of directors has a compensation committee, audit committee and nominating and corporate governance committee. The board may also establish other committees to assist in the discharge of its responsibilities.

Compensation Committee. Our compensation committee consists of Dr. Baldino, Mr. McGuire and Ms. Mitchell, each of whom is an independent director. Mr. McGuire serves as chairperson of the compensation committee. Our compensation committee reviews and makes recommendations to our board of directors regarding the compensation and benefits of our executive officers and senior management, establishes and generally reviews policies relating to compensation and benefits applicable to our employees and consultants and administers our incentive compensation and benefit plans, including our 2003 Stock Option and Incentive Plan.

Audit Committee. Our audit committee consists of Dr. Baldino, Mr. Greenacre and Ms. Mitchell, each of whom is an independent director. Mr. Greenacre serves as chairperson of the audit committee. We believe that each of the members of the audit committee is financially sophisticated and is able to read and understand our consolidated financial statements. We believe that Mr. Greenacre is an "audit committee financial expert" as defined in recently adopted SEC rules. Our audit committee makes recommendations to our board of directors regarding the selection of our independent auditors, reviews the independence of such auditors, reviews the results and scope of the audit and other services provided by our independent auditors, reviews the professional fees payable to our independent auditors and reviews and evaluates our internal accounting procedures and controls. Deloitte & Touche LLP currently serves as our independent auditor.

Nominating and Corporate Governance Committee. Our nominating and corporate governance committee consists of Dr. Baldino and Mr. Greenacre, each of whom is an independent director. Mr. Greenacre serves as chairperson of the nominating and corporate governance committee. Our nominating and corporate governance committee reviews and makes recommendations to the board regarding board composition and structure, criteria for board membership and policies relating to the recruitment of board members, assists in identifying and evaluating candidates to be potential new members of the board and oversees the development of policies and processes regarding principles of corporate governance.

Director Compensation

We pay each of our independent directors who is not the direct or indirect beneficial owner of 5% or more of our common stock, or the affiliate of any such 5% holder, an annual retainer for board membership of $20,000 and an annual retainer for each committee membership of $2,500. These independent directors also receive a fee of $1,000 for each board or committee meeting attended in person and a fee of $600 for each board or committee meeting attended via telephone conference call, provided that the cumulative amount of such meeting fees shall not exceed $1,000 per day.

In addition, each of these independent directors who serves on our audit committee will receive on an annual basis an option to purchase 6,667 shares of our common stock and each other of these independent directors will receive on an annual basis an option to purchase 5,000 shares of our common stock, in each case effective immediately following our annual meeting of stockholders. These options will vest in equal monthly installments over a one year period. Upon the initial election or appointment of any of these independent directors to the board of directors, such independent director shall receive an option to purchase 6,667 shares of our common stock, subject to vesting in equal monthly installments over a four year period.

All of our directors will be reimbursed for out-of-pocket expenses incurred on our behalf, and all of our directors are eligible to participate in the 2003 Stock Option and Incentive Plan on an ad hoc basis from time to time at the discretion of the board of directors.

In June 2001 and February 2003, Dr. Baldino acquired 6,667 and 6,000 shares, respectively, of our common stock. In August 2001 and February 2003, Mr. Greenacre acquired 6,667 and 6,000 shares, respectively, of our common stock. These shares were acquired in consideration of services rendered to us. These shares are subject to our right of repurchase in the event the director ceases to serve on our board of directors. This right of repurchase lapses ratably over a 48-month period with respect to the shares granted in 2001 and over a 40-month period with respect to the shares granted in 2003.

Compensation Committee Interlocks and Insider Participation

Our compensation committee consists of Dr. Baldino, Mr. McGuire and Ms. Mitchell. None of our executive officers has served as a director or member of the compensation committee, or other committee serving an equivalent function, of any other entity, whose executive officers served as a director or member of our compensation committee.

Executive Officers

Each of our executive officers has been elected by our board of directors and serves until his or her successor is duly elected and qualified.

Executive Compensation

The following table sets forth the compensation paid to our Chief Executive Officer and each of our other two most highly-compensated executive officers who were serving as executive officers as of December 31, 2002, together with one additional individual for whom disclosure would have been provided had that individual continued serving as an executive officer through December 31, 2002, and whose total compensation exceed $100,000 during the fiscal year ended December 31, 2002. We refer to these individuals as our "named executive officers."

Summary Compensation Table

Name and Principal Position	Annual Compensation(1)		Long-Term Compensation Awards(2)	All Other Compensation($)
	Salary($)	Bonus($)	Securities Underlying Options(#)	
Sherri C. Oberg President and Chief Executive Officer	$250,000	—	129,376	$ —
Howard Bernstein Senior Vice President of Research and Development	221,610	—	68,168	—
Michael R. Slater Senior Vice President of Operations	200,000	—	25,834	—
James R. Fitzgerald, Jr.(3) Former Senior Vice President and Chief Financial Officer	221,738	—	—	106,000

(1) The compensation in this table does not include medical, group life insurance and other benefits received by the named executive officers which are available generally to all of our salaried employees and certain perquisites and other personal benefits received by the named executive officers which do not exceed the lesser of $50,000 or 10% of any such named executive officer's total compensation reported in this table.

(2) The exercise price of these stock option awards is equal to the fair market value of the common stock, as determined by our board of directors contemporaneously with the grant. In the absence of a public trading market for our common stock, our board of directors considered numerous objective and subjective factors in determining the fair market value of our common stock, including the superior rights and preferences of our then outstanding convertible preferred stock, the status of private and public financial markets, valuations of comparable private and public companies, our existing financial resources, a general assessment of future business risks and other factors.

(3) Mr. Fitzgerald's employment with us terminated effective November 1, 2002. In connection with such termination, Mr. Fitzgerald received a severance payment of $106,000.

Option Grants in Last Fiscal Year and Option Values at Fiscal Year End

The following table sets forth information concerning the stock option grants made to each of the named executive officers during the fiscal year ended December 31, 2002. We have never granted any stock appreciation rights. The potential realizable value is calculated based on the term of the option at its time of grant which is ten years. This value is based on assumed rates of stock appreciation of 5% and 10% compounded annually from the date the options were granted until their expiration date, assuming an exercise price equal to the initial public offering price of $14.00, minus the applicable per share exercise price. These numbers are calculated based on the requirements of the SEC and do not reflect our estimate of future stock price growth. Actual gains, if any, on stock option exercises will depend on the future performance of the common stock and the date on which the options are exercised.

Name	Number of Securities Underlying Options Granted	Percent of Total Options Granted to Employees in Fiscal Year	Exercise Price Per Share	Expiration Dates	Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Term	
					5%	10%
Sherri C. Oberg	9,457	2.6%	$0.84	01/01/2012	$ 207,719	$ 335,462
	119,919	32.7	0.84	07/19/2012	2,633,964	4,253,814
Howard Bernstein	8,334	2.3	7.20	01/01/2012	130,048	242,623
	59,834	16.3	0.84	07/19/2012	1,314,225	2,122,455
Michael R. Slater	8,334	2.3	7.20	01/01/2012	130,048	242,623
	17,500	4.8	0.84	07/19/2012	384,379	620,767
James R. Fitzgerald, Jr.	—	—	—	—	—	—

Aggregated Option Exercises in Last Fiscal Year and Fiscal Year End Option Values

The following table sets forth certain information regarding the number and value of options exercised by each of the named executive officers as of December 31, 2002 and the number and value of unexercised options held by each of the named executive officers as of December 31, 2002. There was no public market for our common stock as of December 31, 2002. Accordingly, amounts described in the following table under the heading "Value of Unexercised In-the-Money Options at Year End" are determined by multiplying the number of shares underlying the options by the difference between the initial public offering price of $14.00 per share and the per share option exercise price.

Name	Number of Shares of Common Stock Underlying Unexercised Options at Year End		Value of Unexercised In-the-Money Options at Year End	
	Exercisable	Unexercisable	Exercisable	Unexercisable
Sherri C. Oberg	49,517	158,649	$462,029	$1,809,175
Howard Bernstein	71,383	80,338	838,548	898,478
Michael R. Slater	11,006	39,828	86,416	370,555
James R. Fitzgerald, Jr.	14,300	31,534	97,240	214,431

Employee Benefit Plans

2003 Stock Option and Incentive Plan. In July 2003, our board of directors approved our 2003 Stock Option and Incentive Plan, to become effective on the closing of the offering. The aggregate number of shares of common stock which may be issued under the 2003 Stock Option and Incentive Plan is 2,500,000 shares.

Under the 2003 Stock Option and Incentive Plan, we are authorized to grant incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, to employees and non-qualified stock options, awards of common stock and opportunities to make direct purchases of common stock to our employees, officers, directors and consultants. The maximum number of shares that may be granted to any employee under the 2003 Stock Option and Incentive Plan shall not exceed 583,334 shares of common stock during any calendar year.

The 2003 Stock Option and Incentive Plan is administered by the board of directors or its committee. Subject to the provisions of the 2003 Stock Option and Incentive Plan, the board of directors or its committee each has the authority to select the persons to whom awards are granted and determine the terms of each award, including the number of shares of common stock to be consistent with Section 422 of the Internal Revenue Code and Rule 16b-3 under the Securities and Exchange Act of 1934. Unless otherwise permitted by us, awards are not assignable or transferable except by will or the laws of descent and distribution.

Each of the board of directors or its committee may, in its sole discretion, amend, modify or terminate any award granted or made under the 2003 Stock Option and Incentive Plan, so long as such amendment, modification or termination would not materially and adversely affect the participant. Each of the board or its committee may also, in its sole discretion, accelerate or extend the date or dates on which all or any particular option or options granted under the 2003 Stock Option and Incentive Plan may be exercised.

2003 Employee Stock Purchase Plan. In July 2003, our board of directors approved our 2003 Employee Stock Purchase Plan, to become effective upon the effectiveness of the registration statement of which this prospectus is a part. The purchase plan provides for the issuance of a maximum of 233,334 shares of common stock.

The purchase plan is administered by the board of directors or its committee. Employees who are customarily employed for more than 20 hours per week and for more than 5 months in any calendar year and who have completed more than 90 days of employment on or before the first day of any six-month payment period are eligible to participate in the purchase plan. Outside directors and employees who would own 5% or more of the total combined voting power or value of our stock immediately after the grant may not participate in the purchase plan.

On the first day of a designated payroll deduction or payment period, we will grant to each eligible employee who has elected to participate in the purchase plan an option to purchase shares of our common stock. The employee may authorize between 1% to 10% of his or her total cash compensation to be deducted by us from his or her base pay during the payment period. On the last day of the payment period, the employee is deemed to have exercised the option, at the option exercise price, to the extent of accumulated payroll deductions.

The first payment period will commence on the date on which our common stock is first publicly traded and end on February 29, 2004. Thereafter, the payment periods will commence on the first day of September 1 and March 1, and end on the last day of the following February and August, respectively, of each year. In no case shall an employee be entitled to purchase more than 417 shares of common stock in any one payment period. The exercise price for the option granted in each payment period is 85% of the lesser of the average market price of the common stock on the first or last business day of the payment period, in either event rounded up to the nearest cent.

If an employee is not a participant on the last day of the payment period, such employee is not entitled to exercise his or her option, and the amount of his or her accumulated payroll deductions will be

refunded. Options granted under the purchase plan may not be transferred or assigned. An employee's rights under the purchase plan terminate upon his or her voluntary withdrawal from the plan at any time or upon termination of employment. No options have been granted to date under the purchase plan.

1994 Stock Plan. Our 1994 Stock Plan was initially approved by our board of directors and was approved by our stockholders on March 7, 1994. As of September 5, 2003 options to purchase 1,161,828 shares of our common stock were outstanding under our 1994 Stock Plan at a weighted average exercise price of $5.19 per share and 89,252 shares were available for grant under the 1994 Stock Plan. Options granted under our 1994 Stock Plan generally vest over four years and terminate on the tenth anniversary of the date of grant.

Under the 1994 Stock Plan, we are authorized to grant incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, to employees and non-qualified stock options and awards of common stock to our employees, officers, directors and consultants.

The 1994 Stock Plan is administered by the board of directors or its committee. Subject to the provisions of the 1994 Stock Plan, the board of directors or its committee each has the authority to select the persons to whom awards are granted and determine the terms of each award, including the number of shares of common stock to be consistent with Section 422 of the Internal Revenue Code and Rule 16b-3 under the Securities Exchange Act of 1934. Unless otherwise permitted by us, awards are not assignable or transferable except by will or the laws of descent and distribution.

Each of the board of directors or its committee may, in its sole discretion, accelerate or extend the date or dates on which all or any particular option or options granted under the 1994 Stock Plan may be exercised.

401(k) Plan. We have a Section 401(k) Retirement Savings Plan. The 401(k) plan is a tax-qualified retirement plan covering all regular employees who are over 21 years of age and who have completed three months of service with us. Under the 401(k) plan, participants may elect to defer a portion of their compensation on a pre-tax basis and have it contributed to the plan. In addition, at the discretion of our board of directors, we may make employer contributions into the 401(k) plan for all eligible employees which would be allocated on the basis of compensation.

Limitation of Liability and Indemnification of Officers and Directors

Our by-laws provide that our directors and officers shall be indemnified to the fullest extent permitted by Delaware law, as it now exists or may in the future be amended, against all expenses and liabilities reasonably incurred in connection with their service for us or on our behalf. We have entered into agreements with our directors and officers that also provide for such indemnification and expenses and liability reimbursement. In addition, our certificate of incorporation provides that our directors will not be personally liable for monetary damages for breaches of their fiduciary duty as directors, unless they violated their duty of loyalty to us or its stockholders, acted in bad faith, knowingly or intentionally violated the law, authorized illegal dividends or redemptions or derived an improper personal benefit from their action as directors. We intend to obtain insurance which insures our directors and officers against certain losses and which insures us against our obligations to indemnify the directors and officers.

RELATED PARTY TRANSACTIONS

Other than compensation agreements and other arrangements which are described as required in "Management" and the transactions described below, since January 1, 2000, there has not been, and there is not currently proposed, any transaction or series of similar transactions to which we were or will be a party in which the amount involved exceeded or will exceed $60,000 and in which any director, executive officer, holder of 5% or more of any class of our capital stock or any member of their immediate family had or will have a direct or indirect material interest.

We believe that we have executed all of the transactions set forth below on terms no less favorable to us than we could have obtained from unaffiliated third parties. It is our intention to ensure that all future transactions between us and our officers, directors and principal stockholders and their affiliates, are approved by a majority of the board of directors, including a majority of the independent and disinterested members of the board of directors, and are on terms no less favorable to us than those that we could obtain from unaffiliated third parties.

Private Placements of Securities

In March 1994, we issued and sold an aggregate of $775,000 of Series A convertible preferred stock at a price of $1.00 per share. In March 1995, we issued and sold an aggregate of $2,675,000 of Series B convertible preferred stock, and in May 1995, we issued and sold an aggregate of $950,000 of Series B convertible preferred stock, in each case, at a price of $1.60 per share. In June 1996, we issued and sold an aggregate of $8,374,999 of Series C convertible preferred stock at a price of $2.14 per share. In November 1997, we issued and sold an aggregate of $10,216,872 of Series D convertible preferred stock at a price of $3.00 per share. In October 1998, we issued and sold an aggregate of $2,500,004 of Series E convertible preferred stock at a price of $3.30 per share. In April, June, July and September 2000, we issued and sold an aggregate of $30,045,313 of Series F convertible preferred stock at a price of $4.75 per share. In June 2001, we issued and sold an aggregate of $6,509,039 of Series I convertible preferred at a price of $4.75 per share. In June 2002, we issued and sold an aggregate of $15,139,111 of Series J convertible preferred stock at a price of $1.41 per share. In April and June 2003, we issued and sold an aggregate of $19,440,342 of 10% convertible promissory notes. Concurrent with the issuance of these promissory notes, we issued for no additional consideration warrants exercisable for 459,569 shares of our common stock assuming an exercise price of $8.46 per share. These notes and shares convert into common stock based upon conversion ratios summarized in the notes to our consolidated financial statements, which conversion ratios were adjusted for our reverse stock split as described therein.

The following table summarizes, on a common stock equivalents basis, the participation by our 5% stockholders and stockholders associated with some of our directors in these private placements.

Purchaser(1)	Total Common Stock Equivalents	Aggregate Consideration Paid	Investment Participation
Stockholders associated with Directors			
Thomas Weisel group(2)	3,172,333	$29,787,293	Series F, I, J and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and related warrants
Bank of America Ventures(3)	1,525,282	12,356,507	Series C, D, E, F, I, J and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and related warrants
Burr, Egan, Deleage group(4)	899,096	9,041,386	Series A, B, C, D, E, F, I, J and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and related warrants
Polaris Venture Partners group(5)	695,744	6,751,503	Series C, D, E, F, I, J and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and related warrants
5% Stockholders			
HBM BioVentures (Cayman) Ltd.(6)	639,382	6,335,061	Series F, I, J and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and related warrants
Audax group(7)	576,070	5,345,060	Series F, J and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and related warrants

(1) See "Principal Stockholders" for more detail on shares held by these purchasers.

(2) Derek Lemke-von Ammon, one of our directors, is a Managing Partner of Thomas Weisel Partners LLC. Consideration paid to us by Thomas Weisel group for our convertible preferred stock, 10% convertible promissory notes and warrants during 2000, 2001, 2002 and 2003 were $14,999,997, $2,500,001, $5,000,000 and $7,287,295, respectively. See "Underwriting."

(3) Kate Mitchell, one of our directors, is the president and managing director of Bank of America Ventures. Consideration paid to us by Bank of America Ventures for our convertible preferred stock, 10% convertible promisory notes and warrants during 2000, 2001, 2002 and 2003 were $1,421,438, $473,100, $2,430,004 and $2,720,657, respectively. Also includes consideration paid to us by BA Venture Partners II for our convertible preferred stock, 10% convertible promissory notes and warrants during 2000, 2001, 2002 and 2003 in the amounts of $157,933, $52,564, $269,999 and $302,293, respectively.

(4) Terrance McGuire, one of our directors, is a general partner of Alta V Management Partners, L.P. Consideration paid to us by Burr, Egan, Deleage group for our convertible preferred stock, 10% convertible promisory notes and warrants during 2000, 2001, 2002 and 2003 were $809,680, $269,487, $1,038,292 and $1,787,820, respectively. Includes 133,753 shares of common stock issued upon conversion in July 2002 of 209,190 shares of Series A convertible preferred stock, 174,325 shares of

Series B convertible preferred stock, 162,920 shares of Series C convertible preferred stock, 133,848 shares of Series D convertible preferred stock, 58,866 shares of Series E convertible preferred stock, 47,544 shares of Series F convertible preferred stock and 15,825 shares of Series I convertible preferred stock.

(5) Terrance McGuire, one of our directors, is a member of Polaris Venture Management Co., L.L.C. Consideration paid to us by Polaris Venture Partners group for our convertible preferred stock, 10% convertible promisory notes and warrants during 2000, 2001, 2002 and 2003 were $438,962, $146,101, $1,000,000 and $1,625,738, respectively.

(6) Consideration paid to us by HBM BioVentures (Cayman) Ltd. for our convertible preferred stock, 10% convertible promissory notes and warrants during 2000, 2001, 2002 and 2003 were $2,999,996, $998,488, $842,544 and $1,494,034, respectively.

(7) Consideration paid to us by the Audax group for our convertible preferred stock, 10% convertible promissory notes and warrants during 2000, 2002 and 2003 were $3,000,000, $1,037,420 and $1,307,639, respectively.

In connection with the above transactions, we entered into agreements with all of the investors that invested in the above listed private placements of convertible preferred stock providing for registration rights with respect to these shares. The most recent such agreement restates the registration rights of all investors and certain other parties. For more information regarding this agreement, see "Description of Capital Stock — Registration Rights."

We paid Thomas Weisel Partners LLC a placement fee of approximately $648,000 in 2002 for work performed in connection with our private financing activities. See "Underwriting — Thomas Weisel Partners LLC and the Qualified Independent Underwriter".

Transactions with our Executive Officers

In April 1996, we entered into a registration rights agreement with our founders, including Sherri Oberg, our President and Chief Executive Officer, pursuant to which we granted Ms. Oberg registration rights with respect to shares of common stock held by her. For more information regarding this agreement, see "Description of Capital Stock — Registration Rights."

In September 2001, we entered into an employment agreement with James Fitzgerald, our former Senior Vice President and Chief Financial Officer. Mr. Fitzgerald's employment with us was terminated on November 1, 2002. In accordance with his employment agreement, Mr. Fitzgerald was paid $106,000 in severance pay as a result of such termination.

In July 2003, we entered into indemnification agreements with each of our executive officers and certain other employees providing for indemnification against expenses and liabilities reasonably incurred in connection with their service for us or on our behalf. For more information regarding these agreements, see "Management — Limitation of Liability and Indemnification of Officers and Directors."

Stock Option Awards

For information regarding stock options and stock awards granted to our directors and named executive officers, see "Management — Director Compensation" and "Management — Executive Compensation."

In February 2003, we granted options to purchase 33,334 shares of common stock to Ms. Oberg, options to purchase 25,000 shares of common stock to Dr. Bernstein, options to purchase 8,334 shares of common stock to Mr. Slater and options to purchase 90,000 shares of common stock to Mr. Thero, each at an exercise price of $0.84 per share. In September 2003, we granted options to purchase 122,537 shares of common stock to Ms. Oberg, options to purchase 43,177 shares of common stock to Dr. Bernstein, options to purchase 90,000 shares of common stock to Mr. Cox, options to purchase 15,271 shares of common stock to Mr. Slater and options to purchase 11,361 shares of common stock to Mr. Thero, each at an exercise price of $13.02 per share.

PRINCIPAL STOCKHOLDERS

The following table shows information with respect to the beneficial ownership of our common stock as of September 5, 2003 and as adjusted to reflect the sale of common stock being offered in this offering, by:

- each person or group of affiliated persons known by us to be the beneficial owner of more than 5% of our common stock;
- each of our directors;
- each person who is named in the summary compensation table; and
- all directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. The information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, the number of shares of common stock deemed outstanding includes shares issuable upon exercise of options and warrants held by the respective person or group which may be exercised or converted within 60 days after September 5, 2003. For purposes of calculating each person's or group's percentage ownership, stock options and warrants exercisable within 60 days after September 5, 2003 are included for that person or group but not the stock options or warrants of any other person or group.

Percentage of beneficial ownership before the offering is based on 10,520,797 shares of common stock outstanding as of September 5, 2003, assuming the conversion of all of our outstanding convertible preferred stock and 10% convertible promissory notes, including interest accrued thereon through September 5, 2003, and 14,270,797 shares of common stock outstanding after completion of this offering.

Unless otherwise indicated and subject to applicable community property laws, to our knowledge, each stockholder named in the following table possesses sole voting and investment power over the shares listed, except for those jointly owned with that person's spouse. Unless otherwise noted below, the address of each person listed on the table is c/o Acusphere, Inc., 500 Arsenal Street, Watertown, Massachusetts 02472.

		Percent of Common Stock Outstanding	
Name and Address of Beneficial Owner	Shares Held(1)	Before Offering	After Offering
Thomas Weisel group(2) One Montgomery Street Suite 3700 San Francisco, California 94104	3,172,333	29.7%	22.0%
Bank of America Ventures(3) 950 Tower Lane Suite 700 Foster City, California 94404	1,525,282	14.4	10.6
Burr, Egan, Deleage group(4) One Post Office Square Boston, Massachusetts 02109	899,096	8.5	6.3
Polaris Venture Partners group(5) 1000 Winter Street Suite 3350 Waltham, Massachusetts 02154	695,744	6.6	4.9
HBM BioVentures (Cayman) Ltd.(6) Eucalyptus Building, Crewe Road Grand Cayman, Cayman Islands	639,382	6.1	4.5
Audax group(7) 101 Huntington Avenue Boston, Massachusetts 02199x	576,070	5.5	4.0
Sherri C. Oberg(8)	240,479	2.3%	1.7%
Howard Bernstein(9)	120,735	1.1	*
Michael R. Slater(10)	23,977	*	*

Name and Address of Beneficial Owner	Shares Held(1)	Percent of Common Stock Outstanding	
		Before Offering	After Offering
James R. Fitzgerald, Jr.(11)	—	—	—
Frank Baldino, Jr.(12)	12,667	*	*
Martyn Greenacre(13)	12,667	*	*
Derek Lemke-von Ammon(14)	3,172,333	29.7	22.0
Terrance McGuire(15)	1,594,840	15.0	11.1
Kate Mitchell(16)	1,372,757	13.0	9.6
All officers and directors as a group (11 persons)(17)	6,571,283	59.4	44.4

* Indicates ownership of less than 1%.

(1) Includes the conversion of our 10% convertible promissory notes, including principal and estimated accrued interest thereon through September 5, 2003, into shares of our common stock effective upon closing of the offering made by this prospectus.

(2) Represents 2,718,311 shares, including 142,450 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners, L.P., 62,802 shares, including 3,291 shares issuable upon exercise of a warrant, beneficially owned by TWP CEO Founder's Circle (AI), L.P., 229,454 shares, including 12,024 shares issuable upon exercise of a warrant, beneficially owned by TWP CEO Founder's Circle (QP), L.P., 63,593 shares, including 3,332 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners (Dutch), L.P., 63,593 shares, including 3,332 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners (Dutch II), L.P., 22,501 shares, including 1,132 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners Employee Fund, L.P., and 12,079 shares beneficially owned by TWP 2000 Co-Investment Fund, L.P. Thomas Weisel Capital Associates is the general partner of each of the Thomas Weisel fund entities. Mr. Lemke, one of our directors, is a managing partner of Thomas Weisel Capital Associates. In such capacity, he may be deemed to share voting and investment power with respect to the shares held by these entities. Mr. Lemke disclaims beneficial ownership of the shares held by these entities, except to the extent of his proportionate pecuniary interest therein. See "Underwriting — Thomas Weisel Partners LLC and the Qualified Independent Underwriter."

(3) Represents 1,372,757 shares, including 61,811 shares issuable upon exercise of a warrant, beneficially owned by Bank of America Ventures, and 152,525 shares, including 6,867 shares issuable upon exercise of a warrant, beneficially owned by BA Venture Partners II. Bank of America Ventures is a wholly owned subsidiary of Bank of America Corporation, which is a publicly traded company on the New York Stock Exchange. BA Venture Partners II is a co-investment general partnership comprised of officers and former officers of Bank of America Ventures. Voting and investment power with respect to the shares held by BA Venture Partners II is determined by the vote of the majority-in-interest of the two partners of BA Venture Partners II that are still employed by Bank of America Ventures. The two partners who have voting and investment power are Rory O'Driscoll and Robert Obuch. Bank of America Ventures disclaims beneficial ownership of the securities owned by BA Venture Partners II. The beneficial ownership of the securities held by BA Venture Partners II may be attributed to Bank of America Ventures, however, due to the employment relationship of the voting general partners of BA Venture Partners II. BA Venture Partners II disclaims beneficial ownership of securities owned by Bank of America Ventures, and BA Venture Partners II has advised us that the beneficial ownership of the securities held by Bank of America Ventures should not be attributed to BA Venture Partners II.

(4) Represents 889,747 shares, including 40,195 shares issuable upon exercise of a warrant, beneficially owned by Alta V Limited Partnership, and 9,349 shares, including 422 shares issuable upon exercise of a warrant, beneficially owned by Customs House Partners. Burr, Egan, Deleage & Co. directly or

indirectly provides investment advisory services to various venture capital funds, including Alta V Limited Partnership and Customs House Partners. Mr. McGuire, one of our directors, is a principal of Burr, Egan, Deleage & Co. and a general partner of Alta V Management Partners, L.P., the general partner of Alta V Limited Partnership. In such capacities, he may be deemed to share voting and investment power with respect to the shares held by Alta V Limited Partnership and Customs House Partners. Mr. McGuire disclaims beneficial ownership of these shares, except to the extent of his proportionate pecuniary interest therein.

(5) Represents 656,400 shares, including 34,850 shares issuable upon exercise of a warrant, beneficially owned by Polaris Venture Partners, L.P., and 39,344 shares, including 2,085 shares issuable upon exercise of a warrant, beneficially owned by Polaris Venture Partners Founders' Fund, L.P. Polaris Venture Management Co., LLC is the general partner of each of the Polaris Venture Partners group entities. Mr. McGuire, one of our directors, is a member of Polaris Venture Management Co., LLC. In such capacity, he may be deemed to share voting and investment power with respect to the shares held by each of the Polaris Venture Partners group entities. Mr. McGuire disclaims beneficial ownership of these shares, except to the extent of his proportionate pecuniary interest therein.

(6) Includes 33,943 shares issuable upon exercise of a warrant beneficially owned by HBM BioVentures (Cayman) Ltd. The board of directors of HBM BioVentures (Cayman) Ltd. has voting and investment power with respect to these shares. The board of directors is comprised of John Arnold, Colin Shaw, Richard Coles, Andreas Wicki and John Urquhart, none of whom has individual voting or investment power with respect to these shares.

(7) Represents 531,121 shares, including 27,408 shares issuable upon exercise of a warrant, beneficially owned by Audax Private Equity Fund, L.P., 24,260 shares, including 1,287 shares issuable upon exercise of a warrant, beneficially owned by Audax Co-Invest, L.P., 7,767 shares, including 5 shares issuable upon exercise of a warrant beneficially owned by Audax Trust Co-Invest, L.P., 9,141 shares, including 843 shares issuable upon exercise of a warrant beneficially owned by AFF Co-Invest L.P. and 3,781 shares, including 164 shares issuable upon exercise of a warrant beneficially owned by Audax Special Purpose Co-Invest, L.P. Audax Private Equity Business, L.L.C. is the general partner of Audax Private Equity Fund, L.P. 101 Huntington Holdings, LLC is the general partner of Audax Co-Invest, L.P., Audax Trust Co-Invest, L.P., AFF Co-Invest, L.P. and Audax Special Purpose Co-Invest, L.P. Audax has informed us that there is no natural person with voting or investment power over these shares.

(8) Includes 99,836 shares issuable to Ms. Oberg upon exercise of stock options. Also includes 16,667 shares held by the AMO Irrevocable Trust — 2000 and 16,667 shares held by the EAO Irrevocable Trust — 2000, for the benefit of Ms. Oberg's two children, respectively, 1,667 shares held by Lambert R. Oberg and Jean P. Oberg, the in-laws of Ms. Oberg, and 1,667 shares held by Mary C. Carroll and A. David Carroll, the parents of Ms. Oberg. Ms. Oberg disclaims beneficial ownership of these shares. Ms. Oberg's address is c/o Acusphere.

(9) Includes 95,283 shares issuable to Dr. Bernstein upon exercise of stock options. Dr. Bernstein's address is c/o Acusphere.

(10) Represents 23,977 shares issuable to Mr. Slater upon exercise of stock options. Mr. Slater's address is c/o Acusphere.

(11) Mr. Fitzgerald's employment with us terminated effective November 1, 2002.

(12) Represents 12,667 shares of restricted common stock subject to vesting. Dr. Baldino's address is c/o Cephalon, Inc., 145 Brandywine Parkway, West Chester, PA 19380.

(13) Represents 12,667 shares of restricted common stock, subject to vesting. Mr. Greenacre's address is c/o Acusphere.

(14) Mr. Lemke is a managing partner for Thomas Weisel Capital Partners. In such capacity, he may be deemed to share voting and investment power with respect to the 2,718,311 shares, including 142,450 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners, L.P., 62,802 shares, including 3,291 shares issuable upon exercise of a warrant, beneficially

owned by TWP CEO Founders Circle (AI), L.P., 229,454 shares, including 12,024 shares issuable upon exercise of a warrant, beneficially owned by TWP CEO Founders Circle (QP), L.P., 63,593 shares, including 3,332 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners (Dutch), L.P., 63,593 shares, including 3,332 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Partners (Dutch II), L.P., 22,501 shares, including 1,132 shares issuable upon exercise of a warrant, beneficially owned by Thomas Weisel Capital Employee Fund, L.P., 12,079 shares beneficially owned by TWP 2000 Co-Investment Fund, L.P. Mr. Lemke disclaims beneficial ownership of the shares held by these funds, except to the extent of his proportionate pecuniary interest therein. Mr. Lemke's address is c/o of Thomas Weisel Capital Partners.

(15) Mr. McGuire, one of our directors, is a principal of Burr, Egan, Deleage & Co. and a general partner of Alta V Management Partners, L.P., the general partner of Alta V Limited Partnership. In such capacities, he may be deemed to share voting and investment power with respect to the 889,747 shares, including 40,195 shares issuable upon exercise of a warrant, beneficially owned by Alta V Limited Partnership and 9,349 shares, including 422 shares issuable upon exercise of a warrant, beneficially owned by Customs House Partners. Mr. McGuire disclaims beneficial ownership of the shares held by Alta V Limited Partnership, except to the extent of his proportionate pecuniary interest therein. He also disclaims beneficial ownership of the shares held by Customs House Partners. Polaris Venture Management Co., L.L.C. is the general partner of both Polaris Venture Partners, L.P. and Polaris Venture Partners Founders' Fund, L.P. Mr. McGuire is a member of Polaris Venture Management Co., L.L.C. In such capacity, he may be deemed to share voting and investment power with respect to the 656,400 shares, including 34,850 shares issuable upon exercise of a warrant, beneficially owned by Polaris Venture Partners, L.P. and 39,344 shares, including 2,085 shares issuable upon exercise of a warrant, beneficially owned by Polaris Venture Partners Founders' Fund, L.P. Mr. McGuire disclaims beneficial ownership of these shares, except to the extent of his proportionate pecuniary interest therein. Mr. McGuire's address is c/o Polaris Ventures.

(16) Ms. Mitchell is the president and managing director of Bank of America Ventures. In such capacity, she may be deemed to share voting and investment power with respect to the 1,372,757 shares, including 61,811 shares issuable upon exercise of a warrant, beneficially owned by Bank of America Ventures, and the beneficial ownership of such securities may be attributable to Ms. Mitchell. Ms. Mitchell disclaims beneficial ownership of these shares, except to the extent of her proportionate pecuniary interest therein. Ms. Mitchell is not a partner of BA Venture Partners II and has no voting or investment power with respect to the 152,525 shares, including 6,867 shares issuable upon exercise of a warrant, beneficially owned by BA Venture Partners II. Consequently, Ms. Mitchell has advised us that the beneficial ownership of the securities held by BA Venture Partners II should not be attributed to her. Ms. Mitchell's address is c/o Bank of America Ventures.

(17) Includes an aggregate of 544,848 shares issuable upon exercise of stock options and warrants.

DESCRIPTION OF CAPITAL STOCK

General

Following this offering, our authorized capital stock will consist of 98,500,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of undesignated preferred stock, par value $0.01 per share, issuable in one or more series designated by our board of directors. No other class of capital stock will be authorized.

As of September 5, 2003, there were approximately 96 holders of record of our capital stock. Immediately prior to the closing of the offering, all outstanding shares of convertible preferred stock and 10% convertible promissory notes, including interest accrued thereon, will be converted into common stock.

The following summary description of our capital stock, certificate of incorporation and by-laws is not intended to be complete and assumes the filing as of the closing of the offering of our amended and restated certificate of incorporation. This description is qualified by reference to the provisions of applicable law and to our certificate of incorporation and by-laws filed as exhibits to the registration statement of which this prospectus is a part.

Common Stock

As of September 5, 2003, there were 10,520,797 shares of common stock outstanding held of record by 96 stockholders, including 1,993,632 shares of common stock outstanding prior to this offering and 27,413,080 shares of preferred stock, after giving effect to the conversion of all of our outstanding shares of convertible preferred stock and upon conversion of all of our outstanding 10% convertible promissory notes including interest accrued through September 5, 2003. In addition, we have reserved an aggregate of 1,161,828 shares of common stock upon exercise of options outstanding under our 1994 Stock Plan and 89,252 shares of common stock available for issuance under the 1994 Stock Plan, 2,500,000 shares of common stock for issuance under our 2003 option plan, 233,334 shares of common stock for issuance under our 2003 purchase plan, 581,825 shares of common stock for issuance upon the exercise of outstanding stock purchase warrants and 89,605 shares issuable upon exercise of a purchase option that will expire upon completion of the offering made by this prospectus.

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. Directors are elected by a plurality of the votes of the shares present in person or by proxy at the meeting and entitled to vote in such election. Holders of common stock are entitled to receive ratably any dividends as may be declared by the board of directors out of funds legally available distribution, after provision has been made for any preferential dividend rights of outstanding preferred stock, if any. Upon our liquidation, dissolution or winding up, the holders of common stock are entitled to receive ratably the net assets available after the payment of all of our debts and other liabilities, and after the satisfaction of the rights of any outstanding preferred stock, if any. Holders of the common stock have no preemptive, subscription, redemption or conversion rights. The rights, powers, preferences and privileges of holders of common stock are subordinate to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Following this offering, our board of directors will be authorized, without further vote or action by the stockholders, to issue from time to time up to an aggregate of 5,000,000 shares of preferred stock in one or more series. Each series of preferred stock shall have such number of shares, designations, preferences, voting powers, qualifications and special or relative rights or privileges as shall be determined by our board of directors, which may include, among others, dividend rights, voting rights, redemption and sinking fund provisions, liquidation preferences, conversion rights and preemptive rights.

The issuance of preferred stock, while providing desired flexibility in connection with possible acquisitions and other corporate purposes, could adversely affect the voting power or other rights of the holders of common stock, and could make it more difficult for a third party to acquire, or could discourage a third party from attempting to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock after the offering.

Warrants

As of June 30, 2003, we had outstanding warrants to purchase an aggregate of 581,825 shares of common stock at an effective weighted average exercise price of $10.64 per share as follows:

Number of Shares	Exercise Price	Expiration Date
8,601	$ 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
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
452,029	$ 8.46	April 11, 2008
7,540	$ 8.46	June 27, 2008

In addition, an option to purchase 89,605 shares at an effective exercise price of $16.74 per share was outstanding as of September 5, 2003, which option will expire upon completion of the offering made by this prospectus.

Each of these warrants includes a cashless exercise feature, and the holders are entitled to customary antidilution protection, including adjustments to the number of shares of common stock issuable upon exercise of the warrants in the event of a subdivision or combination of our common stock or the payment of a stock dividend on our common stock.

Registration Rights

Pursuant to the terms of a registration rights agreement, after this offering, the holders of approximately 10,348,056 shares of common stock and warrants to acquire 518,551 shares of common stock will be entitled to certain rights with respect to the registration of such shares under the Securities Act. Under the terms of the registration rights agreement, if we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, the holders are entitled to notice of such registration and are entitled to include shares of their common stock therein. Additionally, the holders are entitled to certain demand registration rights pursuant to which they may require us to file a registration statement under the Securities Act at our expense with respect to their shares of common stock, and we are required to use our best efforts to effect that registration. We are not required to effect more than four of these demand registrations. In addition, the holders are entitled to registration rights pursuant to which they may require us to file a registration statement under the Securities Act on Form S-3 at our expense with respect to their shares of common stock, and we are required to use our best efforts to effect that registration. All of these registration rights are subject to conditions and limitations, including the right of the underwriters of an offering to limit the number of shares included in such registration and our right not to effect a requested registration within six months following this offering. In addition, our obligation to register shares of common stock terminates

immediately with respect to a security holder holding 3% or less of our outstanding shares, provided that all shares held by the holder may be publicly sold within a three-month period pursuant to the Securities Act. In any event, all registration rights terminate five years from the date of this prospectus.

Anti-Takeover Effects of Provisions of Delaware Law and Our Certificate of Incorporation and By-laws

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" is defined as a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. Subject to various exceptions, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within the past three years did own, 15% or more of a corporation's voting stock. This statute could prohibit or delay the accomplishment of mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

In addition, some provisions of our certificate of incorporation and by-laws may be deemed to have an anti-takeover effect and may delay, defer or prevent a tender offer or takeover attempt that a stockholder might deem to be in his or her best interest. The existence of these provisions could limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions include:

Stockholder Action; Special Meeting of Stockholders. Our certificate of incorporation provides that stockholders may not take action by written consent, but only at a duly called annual or special meeting of stockholders. The certificate of incorporation further provides that special meetings of our stockholders may be called only by the chairman of the board of directors or a majority of the board of directors, and in no event may the stockholders call a special meeting. Thus, without approval by the chairman of the board of directors or a majority of the board of directors, stockholders may take no action between meetings.

Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our by-laws provide that a stockholder seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at an annual meeting of stockholders, must provide timely notice of this intention in writing. To be timely, a stockholder's notice must be delivered to our secretary at our principal executive offices not less than 120 days prior to the first anniversary of the date of our notice of annual meeting provided with respect to the previous year's annual meeting of stockholders. However, if no annual meeting of stockholders was held in the previous year or the date of the annual meeting of stockholders has been changed to be more than 30 calendar days from the time of the previous year's annual meeting, then a proposal shall be received no later than the later of the close of business on the sixtieth day prior to such annual meeting or on the tenth day following the date on which notice of the date of the meeting was mailed or a public announcement was made. The amended and restated by-laws also include a similar requirement for making nominations at special meetings and specify requirements as to the form and content of a stockholder's notice. These provisions may preclude stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual or special meeting of stockholders.

Authorized but Unissued Shares. The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the Nasdaq National Market. These additional shares may be utilized for a variety of corporate acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Super-majority Voting. Delaware law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws requires a greater percentage. We have provisions in our certificate which require 75% of the voting power of all of the then outstanding shares of our capital stock to amend or repeal certain provisions in our certificate of incorporation which include, but is not limited to provisions which would reduce or eliminate the number of authorized common or preferred shares and all indemnification provisions. We also have provisions in our certificate which require 75% of the voting power of all of the then outstanding shares of our capital stock to adopt, amend or repeal any provision of our by-laws.

Staggered Board. Our certificate of incorporation and by-laws provide for the division of our board of directors into three classes, as nearly equal in size as possible, with staggered three-year terms. In addition, our certificate of incorporation and by-laws provide that directors may be removed without cause only by the affirmative vote of the holders of 75% of the shares of capital stock entitled to vote for the election of directors at an election of directors. Any one or more or all of the directors may be removed with cause only by the holders of at least a majority of the shares then entitled to vote at an election of directors. Under our certificate of incorporation and by-laws, any vacancy on the board of directors, for the election of directors, including a vacancy resulting from an enlargement of the board, may only be filled by vote of a majority of the directors then in office. The classification of the board of directors and the limitations on the removal of directors and filling of vacancies would have the effect of making it more difficult for a third party to acquire control of us, or of discouraging a third party from acquiring control of us.

Limitation of Liability

Our certificate of incorporation provides that no director shall be personally liable to us or to our stockholders for monetary damages for breach of fiduciary duty as a director, except that the limitation shall not eliminate or limit liability to the extent that the elimination or limitation of such liability is not permitted by the Delaware General Corporation Law as the same exists or may hereafter be amended.

Our by-laws further provide for the indemnification of our directors and officers to the fullest extent permitted by Section 145 of the Delaware General Corporation Law, including circumstances in which indemnification is otherwise discretionary. A principal effect of these provisions is to limit or eliminate the potential liability of our directors for monetary damages arising from breaches of their duty of care, subject to certain exceptions. These provisions may also shield directors from liability under federal and state securities laws.

Transfer Agent and Registrar

Upon the closing of this offering, the transfer agent and registrar for the common stock will be American Stock Transfer & Trust Company.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and we cannot assure you that a significant public market for our common stock will develop or be sustained after this offering. Future sales of significant amounts of our common stock, including shares of our outstanding common stock and shares of our common stock issued upon exercise of outstanding options and warrants, in the public market after this offering could adversely affect the prevailing market price of our common stock and could impair our future ability to raise capital through the sale of our equity securities.

Sale of Restricted Shares and Lock-Up Agreements

Upon completion of this offering, we will have outstanding 14,270,797 shares of common stock based upon our shares outstanding as of September 5, 2003, and assuming:

- no exercise of the underwriters' over-allotment option; and
- no exercise of outstanding options or warrants after September 5, 2003 and prior to completion of this offering.

Of these shares, the 3,750,000 shares of common stock sold in this offering and any shares issued upon exercise of the underwriters' over-allotment option will be freely tradable without restriction under the Securities Act, unless purchased by our affiliates, as that term is defined in Rule 144 under the Securities Act.

The remaining 10,520,797 shares of common stock were issued and sold by us in private transactions, and are eligible for public sale if registered under the Securities Act or sold in accordance with Rules 144, 144(k) or 701 of the Securities Act. However, 10,375,743 of these remaining shares of common stock are held by officers, directors, and existing stockholders who are subject to various 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 a period of 180 days after the date of this prospectus without the prior written consent of SG Cowen Securities Corporation. SG Cowen may, in its sole discretion and at any time without notice, release all or any portion of the common stock held by our officers, directors, and existing stockholders subject to these lock-up agreements.

As of the date of this prospectus up to 142,169 of the remaining shares may be eligible for sale in the public market. Beginning 180 days after the date of this prospectus, 8,130,524 of these remaining shares will be eligible for sale in the public market, although all but 2,077,224 shares will be subject to certain volume limitations under Rule 144.

Upon the closing of this offering, options to purchase 1,161,828 shares of common stock will be held by existing optionees, based on options outstanding on September 5, 2003. Under the terms of their option agreements, holders of all of these options have agreed to be bound by a 180 day lock-up.

Rule 144

In general, Rule 144 allows a stockholder (or stockholders where shares are aggregated) who has beneficially owned shares of our common stock for at least one year and who files a Form 144 with the SEC to sell within any three month period commencing 90 days after the date of this prospectus a number of those shares that does not exceed the greater of:

- 1% of the number of shares of common stock then outstanding, which will equal approximately 142,708 shares immediately after this offering; or
- the average weekly trading volume of the common stock during the four calendar weeks preceding the filing of the Form 144 with respect to such sale.

Sales under Rule 144, however, are subject to specific manner of sale provisions, notice requirements, and the availability of current public information about us. We cannot estimate the number of shares of common stock our existing stockholders will sell under Rule 144, as this will depend on the market price for our common stock, the personal circumstances of the stockholders, and other factors.

Rule 144(k)

Under Rule 144(k), in general, a stockholder who has beneficially owned shares of our common stock for at least two years and who is not deemed to have been an affiliate of our company at any time during the immediately preceding 90 days may sell shares without complying with the manner of sale provisions, notice requirements, public information requirements, or volume limitations of Rule 144. Affiliates of our company, however, must always sell pursuant to Rule 144, even after the otherwise applicable Rule 144(k) holding periods have been satisfied.

Rule 701

Rule 701 generally allows a stockholder who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been an affiliate of our company during the immediately preceding 90 days to sell these shares in reliance upon Rule 144, but without being required to comply with the public information, holding period, volume limitation, or notice provisions of Rule 144. Rule 701 also permits affiliates of our company to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701.

As of September 5, 2003, 172,725 shares of our outstanding common stock had been issued in reliance on Rule 701 as a result of exercises of stock options and stock awards.

Registration Rights

Our existing stockholders holding approximately 10,348,056 shares of our common stock have the right, subject to various conditions and limitations, to demand the filing of and include their shares in registration statements relating to our securities. By exercising their registration rights and causing a large number of shares to be registered and sold in the public market, these holders could cause the price of the common stock to fall. In addition, any demand to include such shares in our registration statements could have a material adverse effect on our ability to raise needed capital.

Options and Warrants

In addition to the 14,270,797 shares of common stock outstanding immediately after this offering, as of September 5, 2003, there were outstanding options to purchase 1,161,828 shares of our common stock and outstanding warrants to purchase up to 581,825 shares of our common stock and an option to purchase 89,605 shares, which option will expire upon completion of the offering made by this prospectus.

As soon as practicable after the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act covering shares of our common stock issued or reserved for issuance under our 1994 Stock Plan, 2003 Stock Option and Incentive Plan and 2003 Employee Stock Purchase Plan. Accordingly, shares of our common stock registered under such registration statements will be available for sale in the open market upon exercise by the holders, subject to vesting restrictions with us, contractual lock-up restrictions, and/or market stand-off provisions applicable to each option agreement that prohibit the sale or other disposition of the shares of common stock underlying the options for a period of 180 days after the date of this prospectus, if requested by us.

MATERIAL UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF OUR COMMON STOCK

The following discussion of certain United States federal income and estate tax considerations is for general information only. Accordingly, all prospective non-U.S. holders of our common stock are urged to consult their own tax advisors with respect to the United States federal, state and local and foreign tax consequences of the acquisition, ownership and disposition of our common stock.

As used in this prospectus, the term "non-U.S. holder" is a person who is a beneficial owner of our common stock other than:

- a citizen or resident of the United States (within the meaning of Section 7701(b) of the United States Internal Revenue Code of 1986, as amended, or the "Code");
- a corporation, or other entity taxable as a corporation, formed under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to United States federal income taxation regardless of its source; or
- a trust subject to the primary supervision of a court within the United States and the control of one or more United States persons with respect to substantial trust decisions, or a trust (other than a wholly-owned grantor trust) treated as a domestic trust despite not meeting the requirements described above.

Except as specifically described below, this discussion does not address:

- state, local or foreign tax consequences;
- the tax consequences to stockholders, beneficiaries or holders of other beneficial interests in a non-U.S. holder;
- special tax rules that may apply to selected non-U.S. holders, including without limitation, non-U.S. holders of interests in domestic or foreign partnerships, partnerships, banks or other financial institutions, insurance companies, brokers or dealers in securities, traders in securities, tax-exempt entities, pension funds, regulated investment companies and United States expatriates; or
- special tax rules that may apply to a non-U.S. holder that holds our common stock as part of a straddle, hedge, conversion, synthetic security, constructive sale or other risk reduction transaction for United States federal income tax purposes, or a non-U.S. holder that does not hold our common stock as a capital asset within the meaning of Section 1221 of the Code.

The following discussion is based on provisions of the Code, applicable United States Treasury Regulations and administrative and judicial interpretations, all as of the date of this prospectus, and all of which are subject to change, retroactively or prospectively, or to different interpretation. There can be no assurance that the United States Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling from the IRS or an opinion of counsel with respect to the United States federal income or estate tax consequences of the purchase or ownership of our common stock to a non-U.S. holder.

Dividends

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Please see "Dividend Policy." In the event, however, that dividends are paid in cash or property on shares of our common stock, such dividends paid to a non-U.S. holder generally will be subject to withholding of United States federal income tax at a 30% rate or such lower rate as may be provided by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as "effectively connected" with a United States trade or business conducted by a non-U.S. holder (and, if an applicable income tax treaty so provides, are also attributable to a

permanent establishment of such non-U.S. holder), known as "United States trade or business income," are generally exempt from the 30% withholding tax if the non-U.S. holder files the appropriate IRS form with the payor. However, such United States trade or business income, net of specified deductions and credits, is taxed at the same graduated United States federal income tax rates applicable to United States persons. Any United States trade or business income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of United States withholding tax or other exclusion from withholding under an income tax treaty may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the IRS.

Gain on Disposition of Common Stock

A non-U.S. holder generally will not be subject to United States federal income tax with respect to gain realized on the sale, exchange or other disposition of our common stock unless:

- the gain is United States trade or business income, in which case the graduated United States federal income tax rates applicable to United States persons and the branch profits tax described above may apply;
- the non-U.S. holder is an individual who is present in the United States for more than 182 days in the taxable year of the disposition and meets certain other requirements; or
- certain rules (described below) relating to "United States real property holding corporation" status apply to such sale, exchange or other disposition.

Gain recognized on a sale, exchange or other disposition may be subject to United States federal income tax (and, in certain circumstances, to withholding tax) if we are, or have been, a United States real property holding corporation during the shorter of the five-year period ending on the date of such sale, exchange or other disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a United States real property holding corporation if the fair market value of its "United States real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are (or have been) a United States real property holding corporation, or that we are likely to become one in the future.

Federal Estate Tax

The estates of nonresident alien individuals are subject to United States federal estate tax on property with a United States situs. Because we are a United States corporation, our common stock will be United States situs property if owned or treated as owned by an individual who is a non-U.S. holder at the time of death and will be included in the individual's gross estate for United States federal estate tax purposes, unless an applicable estate tax or other treaty provides otherwise.

Information Reporting and Backup Withholding Tax

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions paid to such holder and the tax withheld with respect to such distributions. Dividends paid to non-U.S. holders who are subject to the United States withholding tax, as described above in "Dividends," generally will be exempt from United States backup withholding.

Information reporting and backup withholding (currently at a rate of 28%) will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the United States office of a broker unless the holder certifies its status as a non-U.S. holder and satisfies certain other qualifications, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds where the transaction is effected outside the United States through a non-United States office of a non-United States broker. However, for information reporting purposes, certain brokers with substantial United States ownership or operations generally will be treated in a manner similar to United States brokers. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available under the provisions of a specific treaty or agreement with the tax authorities of the country in which the non-U.S. holder resides or is incorporated.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder will be refunded, or credited against the holder's United States federal income tax liability, if any, provided that the required information or appropriate claim for refund is furnished to the IRS.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to the terms and conditions of the underwriting agreement, the underwriters named below have severally agreed to purchase from us the number of shares of our common stock set forth below opposite their names on the table below at the public offering price, less the underwriting discounts and commissions set forth below.

Name	Number of Shares
SG Cowen Securities Corporation	1,552,500
Thomas Weisel Partners LLC	742,500
U.S. Bancorp Piper Jaffray Inc.	742,500
Friedman, Billings, Ramsey & Co., Inc.	337,500
Roth Capital Partners, LLC	75,000
Jefferies & Co. Inc.	75,000
Merriman Curhan Ford & Co.	75,000
Morgan Keegan & Company, Inc.	75,000
ThinkEquity Partners LLC	75,000
Total	3,750,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares of common stock offered hereby are conditional and may be terminated at their discretion based on their assessment of the state of the financial markets. The obligations of the underwriters may also be terminated upon the occurrence of other events specified in the underwriting agreement. The underwriters are severally committed to purchase all of the shares of common stock being offered by us if any shares are purchased.

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the common stock to securities dealers at the price to the public less a concession not in excess of $0.588 per share. Securities dealers may reallow a concession not in excess of $0.100 per share to other dealers. After the shares of common stock are released for sale to the public, the underwriters may vary the offering price and other selling terms from time to time.

We have granted to the underwriters an option, exercisable not later than 30 days after the date of this prospectus, to purchase up to an aggregate of 562,500 additional shares of common stock at the public offering price set forth on the cover page of this prospectus less the underwriting discounts and commissions. The underwriters may exercise this option only to cover over-allotments, if any, made in connection with the sale of common stock offered hereby. If the over-allotment option is exercised in full, the underwriters will purchase additional common shares from us in approximately the same proportion as shown in the table above.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us.

		Total	
	Per Share	Without Over-Allotment	With Over-Allotment
Public offering price	$14.00	$52,500,000	$60,375,000
Underwriting discounts and commissions(1)	$ 0.98	$ 3,675,000	$ 4,226,250
Proceeds, before expenses, to us	$13.02	$48,825,000	$56,148,750

(1) As a result of purchases of our securities in April 2003 by affiliates of Thomas Weisel Partners LLC, the underwriters are deemed to have received compensation totaling $58,431 pursuant to the rules of the National Association of Securities Dealers, Inc. As used in the above table and elsewhere in this prospectus the term "underwriting discounts and commissions" does not include this additional deemed underwriters' compensation.

We estimate that the total expenses of this offering, excluding underwriting discounts and commissions, will be approximately $1,500,000.

We have agreed to indemnify the underwriters against certain civil liabilities, including liabilities under the Securities Act and liabilities arising from breaches of representations and warranties contained in the underwriting agreement, and to contribute to payments the underwriters may be required to make in respect of any such liabilities.

All of our directors and executive officers, and substantially all of our stockholders and optionholders, have agreed that for a period of 180 days following the date of this prospectus, they will not offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for shares of common stock. SG Cowen Securities Corporation may, in its sole discretion, at any time without prior notice, release, or cause to be released, all or any portion of the shares from the restrictions in any such agreement. We have entered into a similar agreement with SG Cowen, provided we may, without the consent of SG Cowen, grant options and sell shares pursuant to our stock plans. There are no agreements between SG Cowen and any of our stockholders, optionholders or affiliates releasing them from these lock-up agreements prior to the expiration of the 180-day period.

The underwriters may engage in over-allotment, stabilizing transactions, syndicate covering transactions, penalty bids, and passive market making in accordance with Regulation M under the Securities Exchange Act. Over-allotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Covered short sales are sales made in an amount not greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters may close out a covered short sale by exercising its over-allotment option or purchasing shares in the open market. Naked short sales are sales made in an amount in excess of the number of shares available under the over-allotment option. The underwriters must close out any naked short sale by purchasing shares in the open market. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate covering transactions involve purchases of the shares of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the shares of common stock originally sold by such syndicate member is purchased in a syndicate covering transaction to cover syndicate short positions. Penalty bids may have the effect of deterring syndicate members from selling to people who have a history of quickly selling their shares. In passive market making, market makers in the shares of common stock who are underwriters or prospective underwriters may, subject to certain limitations, make bids for or purchases of the shares of common stock until the time, if any, at which a stabilizing bid is made. These stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the shares of common stock to be higher than it would otherwise be in the absence of these transactions. These transactions may be commenced and discontinued at any time.

Prior to this offering, there has been no public market for our common stock. Consequently, the initial public offering price was determined by negotiation between us and the underwriters. The various factors considered in these negotiations included:

- prevailing market conditions;
- the market capitalizations and the states of development of other companies that we and the underwriters believed to be comparable to us;
- estimates of our business potential;
- our results of operations in recent periods;
- the present state of our development; and
- other factors deemed relevant.

Thomas Weisel Partners LLC and the Qualified Independent Underwriter

This offering is being conducted under Rule 2720(c)(3)(A) of the Conduct Rules of the National Association of Securities Dealers, Inc., or the NASD, which provides that when a NASD member firm participates in the offering of equity securities of a company with which the member has a conflict of interest, the initial public offering price can be no higher than that recommended by a "qualified independent underwriter."

Thomas Weisel Partners LLC may be deemed to have a conflict of interest under Rule 2720(b)(7) of the Conduct Rules of the NASD because entities affiliated with Thomas Weisel Partners beneficially owned 29.7% of our common stock as of June 30, 2003. We also paid Thomas Weisel Partners a placement fee of approximately $648,000 in 2002 for work performed on our behalf in connection with our private financing activities. In addition, Derek Lemke-von Ammon, a Managing Partner for Thomas Weisel Capital Partners and Co-Director of Private Equity for Thomas Weisel Partners, has served as one of our directors since 2002. For more information regarding the relationships between us and Thomas Weisel Partners, see "Principal Stockholders" and "Certain Relationships and Related Party Transactions."

On April 11, 2003, Thomas Weisel Capital Partners Employee Fund, L.P., an affiliate of Thomas Weisel Partners LLC, acquired:

- a promissory note that will convert into approximately 3,559 shares of common stock upon the closing of the offering at the public offering price set forth on the front page of this prospectus,
- 15,306 shares of preferred stock which will convert into 5,102 shares of common stock upon the closing of the offering, and
- a warrant convertible into 1,132 shares of common stock at an exercise price equal to the public offering price set forth on the front page of this prospectus.

These securities are deemed to result in underwriters' compensation under the rules of the NASD. The common stock issued upon conversion of the promissory note and the preferred stock and issuable upon exercise of the warrant may not be sold, transferred, pledged or hypothecated by the fund for a one-year period following the effective date of this offering except in accordance with the NASD rules.

SG Cowen is serving as the qualified independent underwriter in the offering and will recommend a price in compliance with the requirements of Rule 2720(c)(3)(A) of the Conduct Rules of the NASD. SG Cowen has performed due diligence investigations and reviewed and participated in the preparation of the prospectus and the registration statement of which this prospectus forms a part. SG Cowen will receive no additional compensation in its capacity as the qualified independent underwriter.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Testa, Hurwitz & Thibeault, LLP, Boston, Massachusetts. Legal matters in connection with this offering will be passed upon for the underwriters by Hale and Dorr LLP, Boston, Massachusetts.

EXPERTS

The financial statements of Acusphere, Inc. and subsidiaries as of and for the years ended December 31, 2001 and 2002, included in this prospectus and elsewhere in the registration statement have been audited by Deloitte & Touche LLP, independent auditors, as stated in their report appearing herein and elsewhere in the registration statement (which report expresses an unqualified opinion and includes an explanatory paragraph concerning retroactive adjustments to the consolidated financial statements resulting from a reverse stock split and to the application of certain procedures applied to the 2000 consolidated financial statements that were audited by other auditors who have ceased operations and for which Deloitte & Touche LLP have expressed no opinion or other form of assurance other than with respect to

such procedures), and are included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

The financial statements of Acusphere Newco, Ltd. as of December 31, 2000 and 2001 and for the year ended December 31, 2001 and for the period from inception (June 28, 2000) to December 31, 2001, included in this prospectus and elsewhere in the registration statement have been audited by Deloitte & Touche LLP, independent auditors, as stated in their report appearing herein and elsewhere in the registration statement (which report expresses an unqualified opinion and includes an explanatory paragraph referring to Acusphere Newco, Ltd.'s ability to continue as a going concern), and have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

The consolidated financial statements for the year ended December 31, 2000 of Acusphere Inc. included in this prospectus and elsewhere in the registration statement had been audited by Arthur Andersen LLP, independent auditors, as indicated in their report with respect thereto, and are included herein in reliance upon the authority of such firm as experts in accounting and auditing in giving said report. Arthur Andersen LLP has not consented to the inclusion of their report in this prospectus, and we have not obtained their consent to do so in reliance upon Rule 437a of the Securities Act of 1933. We refer you to "Risk Factors — Certain of our financial statements have been audited by Arthur Andersen LLP, and the ability to recover damages from Arthur Andersen may be limited".

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (including the exhibits, schedules, and amendments to the registration statement) under the Securities Act of 1933 with respect to the shares of common stock offered by this prospectus. This prospectus does not contain all the information set forth in the registration statement. For further information with respect to us and the shares of common stock to be sold in this offering, reference is made to the registration statement. Statements contained in this prospectus as to the contents of any contract, agreement, or other document to which we make reference are not necessarily complete. In each instance, we refer you to the copy of such contract, agreement, or other document filed as an exhibit to the registration statement, each such statement being qualified in all respects by the more complete description of the matter involved.

Upon completion of this offering, we will become subject to the reporting and information requirements of the Securities Exchange Act and, as a result, will file periodic and current reports, proxy statements, and other information with the SEC. You may read and copy this information at the Public Reference Room of the SEC located at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. Copies of all or any part of the registration statement may be obtained from the SEC's offices upon payment of fees prescribed by the SEC. The SEC maintains an Internet site that contains periodic and current reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the SEC's website is http://www.sec.gov.

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

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ACUSPHERE NEWCO. LTD.
(A Development Stage Company)

INDEPENDENT AUDITORS' REPORT

To the Board of Directors and Shareholders of
Acusphere, Inc. and Subsidiaries
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, 2001 and 2002, and the related consolidated statements of operations, redeemable convertible preferred stock, stockholders' deficit, and comprehensive loss, and cash flows for the years then ended. 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 consolidated financial statements for the year ended December 31, 2000 and for the period from inception (July 12, 1993) to December 31, 2000 were audited by other auditors who have ceased operations. Those auditors expressed an unqualified opinion on those financial statements in their report dated February 12, 2001.

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, 2001 and 2002, and the results of its operations and its cash flows for the years then ended, 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 year ended December 31, 2000 and 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 13, 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 13 that were applied to revise these financial statements. Our audit procedures included (1) comparing the amounts shown in the loss per share disclosure for 2000 to the Company's underlying accounting analysis obtained from management, (2) comparing the previously reported shares issued and outstanding and statement of operations amounts per the Company's accounting analysis to the previously issued financial statements, and (3) 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 2000 consolidated financial statements or 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
April 11, 2003 (September 12, 2003 as to the effects of the reverse stock split described in Note 13)

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 the years ended December 31, 1998 and 1999 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) equity and cash flows for each of the years in the three-year period ended 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, 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, 2001	As of December 31, 2002	As of June 30, 2003 (Unaudited and Revised)
ASSETS			
CURRENT ASSETS:			
Cash and cash equivalents	$ 6,256,468	$ 7,796,238	$ 11,882,459
Short-term investments	9,342,178	195,698	3,741,629
Due from joint venture	2,371,572	—	—
Other current assets	433,436	428,837	496,265
Total current assets	18,403,654	8,420,773	16,120,353
PROPERTY AND EQUIPMENT, At cost:			
Equipment under capital lease	7,738,551	7,914,614	8,166,803
Laboratory equipment	174,708	806,390	1,330,119
Furniture and fixtures	—	166,926	175,372
Leasehold improvements	1,163,346	98,195	109,751
Total property and equipment	9,076,605	8,986,125	9,782,045
Less accumulated depreciation and amortization	5,231,749	6,202,033	(7,276,646)
Property and equipment, net	3,844,856	2,784,092	2,505,399
OTHER ASSETS	2,208,109	2,162,196	1,779,144
TOTAL	$ 24,456,619	$ 13,367,061	$ 20,404,896
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' DEFICIT			
CURRENT LIABILITIES:			
Convertible notes	$ —	$ —	$ 18,842,842
Current portion of long-term debt	3,155,441	3,564,655	874,228
Accounts payable	1,455,437	737,715	834,415
Accrued expenses	1,078,159	1,219,744	1,521,544
Due to joint venture	1,965,840	—	—
Total current liabilities	7,654,877	5,522,114	22,073,029
LONG-TERM DEBT, Net of current portion	5,290,242	1,725,588	644,235
COMMITMENTS (Notes 9 and 10)			
REDEEMABLE CONVERTIBLE PREFERRED STOCK, At carrying value; including accrued dividends; authorized, 32,106,077 shares; issued and outstanding, 21,214,326 shares as of December 31, 2001, and 31,145,083 shares as of December 31, 2002 and June 30, 2003, respectively	97,739,197	91,467,075	94,702,020
STOCKHOLDERS' DEFICIT:			
Common stock, $0.01 par value; authorized, 11,741,127 shares; issued, 510,905, 1,218,876 and 1,234,679 shares as of December 31, 2001, 2002 and June 30, 2003, respectively; outstanding, 504,878, 1,212,849 and 1,228,652 shares as of December 31, 2001, 2002 and June 30, 2003, respectively	5,109	12,189	12,347
Additional paid-in capital	7,211,698	34,029,519	36,085,143
Less treasury stock, 6,027 shares, at cost	(361)	(361)	(361)
Accumulated other comprehensive income	3,569	288	—
Deferred stock-based compensation	(4,413,493)	(1,793,404)	(2,373,984)
Deficit accumulated during the development stage	(89,034,219)	(117,595,947)	(130,737,533)
Total stockholders' deficit	(86,227,697)	(85,347,716)	(97,014,388)
TOTAL	$ 24,456,619	$ 13,367,061	$ 20,404,896

See notes to consolidated financial statements.

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

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,			Six Months Ended June 30,		Period from Inception (July 12, 1993) to June 30, 2003
	2000	2001	2002	2002	2003	
				(Unaudited)	(Revised)	(Unaudited and Revised)
OPERATING EXPENSES:						
Research and development(1)	$ 9,977,856	$ 11,535,574	$ 13,545,084	$ 7,425,905	$ 6,248,316	$ 64,572,803
General and administrative(1)	2,517,459	3,893,553	3,905,465	1,824,910	1,854,406	17,806,602
Stock-based compensation	15,618	1,075,606	2,195,202	1,121,815	711,813	4,072,346
Total operating expenses	12,510,933	16,504,733	19,645,751	10,372,630	8,814,535	86,451,751
Equity in loss of joint venture	(12,015,000)	(1,965,840)	(1,183,417)	(808,244)	—	(15,164,257)
Interest income	912,428	943,430	223,550	116,436	69,110	3,843,165
Other income	—	—	9,114	8,744	(121,208)	(112,094)
Interest expense	(815,254)	(750,049)	(1,299,746)	(718,070)	(1,040,008)	(5,308,274)
NET LOSS	(24,428,759)	(18,277,192)	(21,896,250)	(11,773,764)	(9,906,641)	(103,193,211)
Accretion of dividends and offering costs on preferred stock	(4,218,395)	(6,248,616)	(6,665,478)	(3,284,086)	(3,234,945)	(27,544,322)
NET LOSS AVAILABLE TO COMMON STOCKHOLDERS	$(28,647,154)	$(24,525,808)	$(28,561,728)	$(15,057,850)	$(13,141,586)	$(130,737,533)
NET LOSS AVAILABLE TO COMMON STOCKHOLDERS PER SHARE — Basic and diluted	$ (64.20)	$ (50.82)	$ (35.40)	$ (30.24)	$ (10.87)	
UNAUDITED PRO FORMA NET LOSS AVAILABLE TO COMMON STOCKHOLDERS PER SHARE — Basic and diluted			$ (3.30)		$ (1.09)	
WEIGHTED-AVERAGE SHARES OUTSTANDING						
Basic and diluted	446,325	482,713	807,119	497,562	1,209,296	
Unaudited pro forma basic and diluted			6,652,651		9,093,418	
(1) Excludes stock-based compensation as follows:						
Research and development	$ 3,203	$ 417,413	$ 915,085	$ 442,403	$ 325,028	$ 1,729,529
General and administrative	12,415	658,193	1,280,117	679,412	386,785	2,342,817
	$ 15,618	$ 1,075,606	$ 2,195,202	$ 1,121,815	$ 711,813	$ 4,072,346

See notes to consolidated financial statements.

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

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' DEFICIT, AND COMPREHENSIVE LOSS
PERIOD FROM INCEPTION (JULY 12, 1993) TO JUNE 30, 2003

	Redeemable Convertible Preferred Stock		Stockholders' Deficit									
			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	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)	
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	
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)

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

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' DEFICIT, AND COMPREHENSIVE LOSS — (Continued)
PERIOD FROM INCEPTION (JULY 12, 1993) TO JUNE 30, 2003

	Redeemable Convertible Preferred Stock		Stockholders' Deficit									
			Common Stock		Additional	Treasury Stock		Accumulated Other	Deferred	Deficit Accumulated	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	During the Development Stage	Stockholders' Deficit	Comprehensive Loss
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	—	—	—	—	—	—	—	—	—	
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	
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)

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

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK, STOCKHOLDERS' DEFICIT, AND COMPREHENSIVE LOSS — (Continued)
PERIOD FROM INCEPTION (JULY 12, 1993) TO JUNE 30, 2003

	Redeemable Convertible Preferred Stock		Stockholders' Deficit									
			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	Comprehensive Loss
	Number of Shares	Carrying Value	Number of Shares	$ 0.01 Par Value		Number of Shares	Cost					
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)	
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 (Unaudited)			847	8	1,881						1,889	
Issuance of restricted common stock (Unaudited)	—	—	14,956	150	31,032	—	—	—	(31,182)	—	—	
Amortization of deferred stock-based compensation (Unaudited)	—	—	—	—	—	—	—	—	711,813	—	711,813	
Unrealized loss on short-term investments (Unaudited)	—	—	—	—	—	—	—	(288)	—	—	(288)	$ (288)
Accretion of dividends and offering costs on preferred stock (Unaudited)	—	3,234,945	—	—	—	—	—	—	—	(3,234,945)	(3,234,945)	
Warrants issued with convertible notes (Unaudited)	—	—	—	—	761,500	—	—	—	—	—	761,500	
Deferred stock-based compensation related to employees (Unaudited)	—	—	—	—	1,396,347	—	—	—	(1,396,347)	—	—	
Reversal of deferred compensation (Unaudited)	—	—	—	—	(135,136)		—	—	135,136	—	—	—
Net loss (Unaudited)	—	—	—	—	—	—	—	—	—	(9,906,641)	(9,906,641)	(9,906,641)
Comprehensive net loss (Unaudited)												$ (9,906,929)
BALANCE, JUNE 30, 2003 (Unaudited) (Revised)	31,145,083	$ 94,702,020	1,234,679	$12,347	$36,085,143	6,027	$(361)	$ —	$(2,373,984)	$(130,737,533)	$(97,014,388)	

Concluded

See notes to consolidated financial statements.

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

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,			Six Months Ended June 30,		Period From Inception (July 12, 1993) to June 30, 2003
	2000	2001	2002	2002	2003	
				(Unaudited)	(Revised)	(Unaudited and Revised)
CASH FLOWS FROM OPERATING ACTIVITIES:						
Net loss	$(24,428,759)	$(18,277,192)	$(21,896,250)	$(11,773,764)	$(9,906,641)	$(103,193,211)
Adjustments to reconcile net loss to net cash used in operating activities:						
Stock-based compensation expense	15,618	1,075,606	2,195,202	1,121,815	711,813	4,072,346
Depreciation and amortization	1,240,596	1,652,334	1,747,372	888,167	1,074,613	8,090,960
Noncash interest expense	131,975	186,050	383,698	207,649	337,237	1,185,979
Noncash rent expense	—	—	53,640	26,820	26,820	80,460
Noncash other expense	—	—	—	—	68,908	68,908
Equity in loss from joint venture	12,015,000	1,965,840	1,183,417	808,244	—	15,164,257
Changes in operating assets and liabilities:						
Due from joint venture	—	(2,371,572)	(777,685)	(776,162)	—	(3,149,257)
Other current assets	(159,994)	(243,070)	4,599	(5,567)	(67,428)	(613,526)
Accounts payable	666,351	333,148	(717,721)	(449,469)	96,700	834,416
Accrued expenses	1,202,609	(533,224)	141,585	966,996	301,800	1,521,545
Net cash used in operating activities	(9,316,604)	(16,212,080)	(17,682,143)	(8,985,271)	(7,356,178)	(75,937,123)
CASH FLOWS FROM INVESTING ACTIVITIES:						
Purchases of property and equipment	(64,868)	(47,153)	(686,613)	(817,473)	(252,551)	(1,495,436)
(Increase) decrease in other assets	(750,814)	(288,033)	(33,640)	319,065	(243,350)	(1,862,376)
Investment in joint venture	(12,015,000)	—	—	—	—	(12,015,000)
Maturities (purchases) of short-term investments	(19,938,153)	11,206,122	9,143,199	8,126,490	(3,546,219)	(3,724,130)
Net cash provided by (used in) investing activities	(32,768,835)	10,870,936	8,422,946	7,628,082	(4,042,120)	(19,096,942)
CASH FLOWS FROM FINANCING ACTIVITIES:						
Payments on long-term debt	(3,106,495)	(4,653,813)	(3,513,221)	(1,499,150)	(3,957,712)	(17,343,841)
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	48,250,347	6,481,694	14,283,074	14,210,566	—	94,337,203
Net proceeds from sale of common stock	32,837	55,406	29,114	13,955	1,889	136,220
Purchase and retirement of treasury stock	—	—	—	—	—	(1,360)
Net cash provided by (used in) financing activities	45,176,689	6,883,287	10,798,967	12,725,371	15,484,519	106,916,524
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	3,091,250	1,542,143	1,539,770	11,368,182	4,086,221	11,882,459
CASH AND CASH EQUIVALENTS, Beginning of period	1,623,075	4,714,325	6,256,468	6,256,468	7,796,238	—
CASH AND CASH EQUIVALENTS, End of period	$ 4,714,325	$ 6,256,468	$ 7,796,238	$ 17,624,650	$11,882,459	$ 11,882,459

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

CONSOLIDATED STATEMENTS OF CASH FLOWS — (Continued)

	Year Ended December 31,			Six Months Ended June 30,		Period From Inception (July 12, 1993) to June 30, 2003
	2000	2001	2002	2002	2003	
				(Unaudited)	(Revised)	(Unaudited and Revised)
SUPPLEMENTAL SCHEDULE OF CASH FLOW INFORMATION:						
Cash paid during the period for interest	$ 682,590	$ 563,999	$ 916,048	$ 510,422	$ 278,087	$ 3,696,922
SUPPLEMENTAL SCHEDULE OF NONCASH FINANCING TRANSACTIONS:						
Equipment acquired under capital lease obligations	$ 1,207,097	$ 3,230,272	$ —	$ —	$ —	$ 8,894,983
Unrealized (loss) gain on investments	$ 16,511	$ (12,942)	$ (3,281)	$ (3,522)	$ (288)	$ —
Warrant issued with facility lease	$ —	$ 536,402	$ —	$ —	$ —	$ 536,402
Discount on long-term debt and capital lease obligations	$ 33,880	$ 673,832	$ —	$ —	$ —	$ 1,018,712
Deferred compensation for services to be performed	$ 165,742	$ 5,340,204	$ —	$ —	$ 1,427,529	$ 6,959,537
Accretion of preferred stock dividends and offering costs	$ 4,218,395	$ 6,248,616	$ 6,665,478	$ 3,284,086	$ 3,234,945	$ 27,544,322
Dividends forfeited on preferred stock conversion	$ —	$ —	$ 2,838,758	$ 2,094,497	$ —	$ 2,838,758
Write-off of net amount due from joint venture	$ —	$ —	$ 371,953	$ —	$ —	$ 371,953
Warrants issued with convertible notes	$ —	$ —	$ —	$ —	$ 761,500	$ 761,500

Concluded

See notes to consolidated financial statements.

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

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.

As shown in the financial statements, the Company has incurred a cumulative net loss of approximately $93.3 million since inception on July 12, 1993, has an accumulated deficit of $117.6 million as of December 31, 2002, and has had no revenues from the sale of products or collaborative arrangements. The Company intends to seek the additional financing it needs to fund its operations. There can be no assurance that such financing will be available with terms acceptable to the Company. However, management believes that its financial resources are sufficient to meet planned operating activities at least through June 30, 2004.

On April 11, 2003, the Company issued secured subordinated convertible promissory notes totaling approximately $19.1 million to certain of its existing shareholders (see Note 13).

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 December 31, 2002 (see Note 4). All intercompany balances and transactions have been eliminated in consolidation.

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. The more significant estimates reflected in these financial statements include judgmental accrued expenses and valuation of stock-based compensation.

Cash, Cash Equivalents, and Short-Term Investments — Cash equivalents consist of short-term, highly liquid investments 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 as of December 31,

2001 and 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 using the straight-line method. Equipment under capital leases and leasehold improvements is depreciated over the shorter of the estimated useful life or remainder of the lease. Laboratory equipment is depreciated over five years. Acusphere reviews its property and equipment whenever events or changes in circumstances indicate that the carrying value of certain assets might not be recoverable and recognizes an impairment loss when it is probable that the estimated cash flows are 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, deferred long-term debt financing costs, 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.

Acusphere relies on certain materials used in its development process, each of which are procured from a single source. 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. 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,		
	2000	2001	2002
Risk-free interest rate	5.17% - 6.50%	3.54% - 4.76%	3.22% - 4.76%
Expected dividend yield	—	—	—
Expected lives	4 years	4 years	4 years
Expected volatility	60%	60%	60%
Weighted-average fair value of options granted	$17.70	$24.48	$4.38

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,			Six Months Ended June 30,	
	2000	2001	2002	2002	2003
				(Unaudited)	
Applicable to common stockholders:					
Net loss — as reported	$(28,647,154)	$(24,525,808)	$(28,561,728)	$(15,057,850)	$(13,141,586)
Add: Stock-based compensation expense included in reported net loss	15,618	1,075,606	2,195,202	1,121,815	711,813
Deduct: Stock-based compensation expense determined under fair value method	(34,517)	(1,364,928)	(2,279,228)	(1,341,791)	(1,008,464)
Net loss — proforma	$(28,666,053)	$(24,815,130)	$(28,645,754)	$(15,277,826)	$(13,438,237)
Net loss per share (basic and diluted):					
As reported	$ (64.20)	$ (50.82)	$ (35.40)	$ (30.24)	$ (10.87)
Pro forma	$ (64.26)	$ (51.42)	$ (35.52)	$ (30.72)	$ (11.11)

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 3,658,597, 4,120,371, and 6,114,942 as of December 31, 2000, 2001, and 2002, 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:

Historical	Year Ended December 31,			Six Months Ended June 30,	
	2000	2001	2002	2002	2003
				(Unaudited)	
Weighted-average common shares outstanding	446,671	490,330	816,720	507,997	1,222,922
Less weighted-average restricted common shares outstanding	(346)	(7,617)	(9,601)	(10,435)	(13,626)
Basic and diluted weighted-average common shares outstanding	446,325	482,713	807,119	497,562	1,209,296

Unaudited Pro Forma Net Loss Per Share — Unaudited pro forma net loss per share is computed using the weighted average number of common shares outstanding, including the pro forma effects of automatic conversion of all outstanding redeemable convertible preferred stock and accrued dividends through each balance sheet date into shares of the Company's common stock effective upon the assumed closing of the Company's proposed initial offering as if such conversions had occurred at the date of original issuance.

The following table reconciles the weighted-average common shares used in the computation of basic and diluted weighted-average common shares outstanding to the unaudited proforma basic and diluted weighted-average common shares outstanding:

	Year Ended December 31, 2002	Six Months Ended June 30, 2003
		(Unaudited)
Basic and diluted weighted-average common shares outstanding	807,119	1,209,296
Weighted-average number of common shares assuming the conversion of all redeemable convertible preferred stock and convertible notes at the date of original issuance	5,845,532	7,884,122
Unaudited proforma weighted-average common shares outstanding	6,652,651	9,093,418

The following table reconciles the net loss available to common stockholders used in the computation of basic and diluted net loss available to common stockholders per share to the unaudited proforma net loss available to common stockholders:

	Year Ended December 31, 2002	Six Months Ended June 30, 2003
		(Unaudited)
Net loss available to common stockholders	$(28,561,728)	$(13,141,586)
Reversal of accretion of dividends and offering costs on preferred stock	6,665,478	3,234,945
Reversal of interest expense on convertible notes	—	424,685
Unaudited proforma net loss available to common stockholders	$(21,896,250)	$ (9,481,956)

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

Unaudited Interim Financial Statements — The consolidated financial statements as of June 30, 2003 and for the six months ended June 30, 2002 and 2003 and the period from inception (July 12, 1993) to June 30, 2003 have been prepared in accordance with generally accepted accounting principles for interim financial information and with Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by generally accepted accounting principles for complete financial statements. In the opinion of management, all adjustments, consisting only of normal and recurring adjustments, considered necessary for a fair presentation of the results of these interim periods have been included. The results of operations for the six months ended June 30, 2003 are not necessarily indicative of the results that may be expected for the full year.

Reclassifications — Certain reclassifications have been made to the 2001 consolidated financial statements to conform to the 2002 presentation.

3. Balance Sheet Data

	As of December 31,	
	2001	2002
Other assets consist of the following:		
Deposits	$1,613,398	$1,647,038
Other assets	594,711	515,158
	$2,208,109	$2,162,196
Accrued expenses consist of the following:		
Accrued contract services	$ 283,350	$ 522,002
Accrued vacation	273,056	315,771
Other accrued expenses	521,753	381,971
	$1,078,159	$1,219,744

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. At the time the joint venture was formed, Elan purchased 1,232,308 shares of Acusphere's Series G Nonvoting Redeemable Convertible Exchangeable Preferred Stock ("Series G Preferred Stock") (see Note 8) for proceeds of $12,015,003. The Series G Preferred Stock was convertible, at Elan's option, into Acusphere's common stock or exchangeable into shares representing a 30.1% interest in the joint venture on a fully diluted basis. Acusphere was contractually obligated to use the proceeds of the Series G Preferred Stock sale to purchase its 80.1% interest in the joint venture on a fully diluted basis. Elan purchased its 19.9% share in the joint venture for $2,984,997. With the proceeds received from Acusphere and Elan, the joint venture purchased a license from Elan for $15,000,000, giving the joint venture rights to use Elan drug delivery technologies. Upon completing this transaction, the cost of this license was expensed as a research

and development cost of Acusphere Newco, Inc. as the technology acquired had not yet reached technological feasibility and there was no future alternative use for the technology.

The joint venture was formed by issuing preferred and common stock valued at $15,000,000 to Acusphere and Elan. 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 consolidated the financial statements of the joint venture but, instead, accounted for its investment in the joint venture under the equity method of accounting.

As of December 31, 2001, the amount due from the joint venture of $2,371,572 represented expenses paid by Acusphere on behalf of the joint venture, which were expected to be reimbursed to Acusphere upon the funding of the joint venture.

In conjunction with a private equity financing completed by Acusphere in July 2002, the Series G Preferred Stock and Series H Preferred Stock then held by Elan and carried at an aggregate value of $21,049,000 were 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 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:

	2001	2002
Capital lease obligations	$3,952,764	$2,342,045
Subordinated loans payable	4,492,919	2,948,198
	8,445,683	5,290,243
Less current maturities	3,155,441	3,564,655
Long-term debt, net	$5,290,242	$1,725,588

Capital Lease Obligations — Acusphere leases capital equipment under various capital lease arrangements. Monthly payments range from $36 to $46,222 with maturities through April 2005. As part of these lease agreements, the leasing companies were granted warrants to purchase an aggregate of 172,990 shares of preferred stock at a purchase price per share equal to the then-current fair value, 25,264 of which are Series F Nonvoting Redeemable Convertible Preferred Stock. 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. Acusphere is amortizing these discounts using the effective-interest-rate method through the respective maturity dates. An aggregate of $79,134 has been recorded as original discount relating to these warrants during the year ending December 31, 2001. During 2000, 2001, and 2002, Acusphere recorded $12,320, $30,580, and $27,503, respectively, in interest expense relating to the amortization of this discount. Interest rates for the above leases range from 6.7% to 8.6%. Acusphere does not have any additional borrowing availability as of December 31, 2002.

Future payments under all capital lease agreements are as follows as of December 31, 2002:

Year Ending December 31,	
2003	$1,373,071
2004	961,257
2005	208,525
Total future minimum lease payments	2,542,853
Less amount representing interest	200,808
Present value of future minimum lease payments	2,342,045
Less current portion of capital leases	1,231,915
Long-term portion of capital leases	$1,110,130

Subordinated Loans Payable — In October 1998, Acusphere entered into a $5,000,000 subordinated loan and security agreement (the "Subordinated Loan Agreement"), as amended, with a financing institution. This loan was paid in full during 2000 and 2001. The note bore interest at 9% per annum. Under the terms of the Subordinated Loan Agreement, the financing institution received an option to purchase up to 349,650 shares of Series E Redeemable Convertible Preferred Stock, under certain circumstances, at any time prior to the earliest of the closing of an initial public offering, the merger or sale of Acusphere, or August 2004, at a per-share price of $4.29, subject to adjustment under certain circumstances, as defined.

As part of the Subordinated Loan Agreement, Acusphere also issued warrants to purchase 75,758 shares of its Series D Redeemable Convertible Preferred Stock and 75,758 shares of its Series E Redeemable Convertible Preferred Stock each at an exercise price of $3.30 per share, subject to adjustment under certain circumstances, as defined. Based on the relative value of the subordinated loan, the deemed value of the warrants, and the purchase option described in the preceding paragraph, Acusphere allocated a total of $311,000 of proceeds to the warrants and to the purchase option. The carrying value of the subordinated loan payable was reduced by the discount. Acusphere is amortizing this discount using the effective-interest-rate method through the maturity date. During 2000, 2001, and 2002, Acusphere recorded $119,655, $44,326, and $0, respectively, in interest expense relating to the amortization of the discount on the subordinated notes.

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 are payable in six, monthly, interest-only payments which began in October 2001 and 24 monthly principal and interest installments thereafter through March 2004. The notes bear interest at 15% per annum. The net carrying amount outstanding at December 31, 2001 and 2002 was $4,492,919 and $2,948,198, respectively.

As part of the notes, Acusphere issued warrants to purchase 136,842 shares of its Series F Nonvoting Preferred Stock at an exercise price of $4.75 per share, 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 is reduced by the

unamortized discount. Acusphere is amortizing this discount using the effective-interest-rate method through the maturity date. During 2001 and 2002, Acusphere recorded $87,617 and $330,279, respectively of interest expense relating to the amortization of the discount on the notes.

Future minimum payments due under the subordinated loans and the notes payable are as follows as of December 31, 2002:

Year Ending December 31,	
2003	$2,332,740
2004	615,458
	$2,948,198

On April 11, 2003, the Company issued secured subordinated convertible promissory notes totaling approximately $19,100,000 to certain of its existing shareholders (see Note 13).

6. Income Taxes

At December 31, 2002, Acusphere had a net operating loss ("NOL") carryforward for income tax purposes of approximately $55,804,000 that expires through 2022. Acusphere also has approximately $2,119,000 of research and development ("R&D") credits as of December 31, 2002 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, 2001 and 2002 are as follows:

	2001	2002
Net operating loss carryforwards	$ 16,137,000	$ 22,321,000
Joint venture loss	5,592,000	6,066,000
Temporary timing differences	5,605,000	7,645,000
Research and development credit carryforwards	1,686,000	2,119,000
Deferred tax asset	29,020,000	38,151,000
Less valuation allowance	(29,020,000)	(38,151,000)
	$ —	$ —

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. The valuation allowance increased by $7,995,000 from December 31, 2000 to 2001.

7. Stockholders' Deficit

Authorized and Reserved Shares — As of December 31, 2002, Acusphere had authorized capital stock of 43,847,204 shares, of which 11,741,127 are $0.01 par value common stock and 32,106,077 are $0.01 par value redeemable convertible preferred stock. After giving effect to the reverse stock split discussed in Note 13, Acusphere has reserved 7,081,363 shares of the authorized 11,741,127 shares of common stock for the conversion of the preferred stock, the issuance of stock options, the exercise of warrants, and the exercise of the purchase option under the Subordinated Loan. Acusphere's authorized and reserved

number of shares were increased in April 2003 in connection with the issuance of the secured subordinated convertible loan agreement (see Note 12).

Common Stock — Acusphere has a right of first refusal to purchase outstanding shares of its common stock, which expires at various times through January 2006, on the subsequent sale of certain shares of common stock held by some of Acusphere's founders. This right automatically terminates upon the closing of an initial public offering that results in aggregate proceeds to Acusphere of at least $7,500,000.

Stock Plan — Acusphere established the 1994 Stock Plan (the "Plan"), which provides that a maximum of 1,008,663 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 Acusphere'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. Acusphere had 120,214 shares available for future stock and option grants under the Plan at December 31, 2002.

Stock option activity under the Plan is 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 (unaudited)	197,726	0.84	0.84
Exercised (unaudited)	(847)	1.26 – 7.20	2.22
Canceled (unaudited)	(45,833)	1.26 – 7.20	7.20
Balance, June 30, 2003 (unaudited)	914,976	0.60 – 7.20	2.63
Exercisable, June 30, 2003 (unaudited)	361,900	$0.60 – $7.20	$3.18
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

During 2000, Acusphere issued 1,667 shares of common stock, 1,369 shares of restricted common stock, and 10,000 options to purchase common stock to nonemployees in consideration of services rendered. During 2001, Acusphere issued 457 shares of restricted common stock to a nonemployee in consideration of services rendered and issued 13,334 shares of restricted common stock during the year ended December 31, 2001 to directors in consideration for past consulting services. The 13,334 shares of restricted stock vest ratably over 48 months. Acusphere has the right to repurchase the unvested portion of the restricted stock at the original issue price should the holders cease to be directors. Acusphere recorded these transactions at fair value, which was $53,822 and $463,839 in 2000 and 2001, respectively. Acusphere has recorded stock-based compensation related to these grants of $10,760, $146,215, and $27,368 during December 31, 2000, 2001 and 2002, respectively. The options to purchase common stock and shares of restricted common stock granted to nonemployees have been issued with various vesting periods ranging from immediate vesting to seven years. 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 invested nonemployee 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 19,667 and 230,119 shares of common stock during the years ended December 31, 2000 and 2001, respectively, at an exercise price and purchase price 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 $0 in 2002 as deferred stock-based compensation and is amortizing this deferred compensation as a charge to operations over the

vesting periods of the options. Acusphere expects to record approximately $868,000, $443,000, and $137,000 of stock-based compensation expense related to the amortization of deferred compensation for the years ending December 31, 2003, 2004, and 2005, respectively.

The following table summarizes information relating to currently outstanding and exercisable options as of December 31, 2002 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	345,399	9.3	$0.72	59,884	$0.84
0.96 - 1.26	49,258	3.8	1.14	49,258	1.14
1.80 - 2.82	72,746	6.1	1.92	67,294	1.92
5.70 - 7.20	296,527	8.6	6.96	109,058	7.08
	763,930			285,494	

8. Redeemable Convertible Preferred Stock

The following table summarizes the activity for the Redeemable Convertible Preferred Stock:

	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	—	—	—	—	—	—	—	—	—	—	—	—

8. Redeemable Convertible Preferred Stock — (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
Accretion of dividends and offering costs	—	2,389	—	4,505	—	1,257,339	—	1,095,078	—	244,412	—	—	—	—	—	—	—	—	—	—	—	—
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

Concluded

On June 17, 2002, the Company entered into an agreement for the sale of Series J and Series J-1 Preferred Stock to existing investors. Under the terms of the agreement, all of the then-outstanding shares of all series of preferred stock were each exchanged for a new series of preferred stock with identical rights and privileges. In addition, existing preferred stockholders who did not participate in the Series J and J-1 financing at 100% of their pro rata share, as defined, were subject to mandatory conversion of a portion or all of their existing preferred stock to common stock. Accordingly, 4,196,456 shares of preferred stock were converted to common stock during 2002 in connection with the Series J financing. To the extent existing preferred stockholders participated at a level in excess of their pro rata share, in addition to being issued Series J shares, the stockholders were issued Series J-1 Preferred Stock in exchange for a portion of their Series B, E and F shares.

The rights, preferences, and privileges of the Series A through J-l Preferred Stock are as follows:

Voting Rights — All holders of preferred stock, have voting rights equal to the number of shares of common stock into which the respective preferred stock is convertible, with the exception of Series F Nonvoting Redeemable Convertible Preferred Stock and Series J-l Redeemable Convertible Preferred Stock. The Series J-l redeemable convertible preferred stock has a lesser proportionate number of voting rights per share.

Dividends — All preferred stockholders are entitled to participate equally on a pro rata basis in any dividend declared for the holders of common stock. From inception to December 31, 2002 no dividends have been declared for holders of common stock. The holders of Series C, D, E, F, and I Preferred Stock are entitled to a cumulative dividend of $0.32 per share annually. The holders of Series J and J-1 Preferred Stock are entitled to a cumulative dividend of $0.11 per share annually. Upon conversion of the preferred stock into common stock, the preferred stockholders forego all cumulative dividends. All dividends have been accrued and included in the carrying value of the redeemable convertible preferred stock in the accompanying consolidated balance sheets. As of December 31, 2002, cumulative accrued dividends on the Company's preferred stock totaled $19,006,000.

Liquidation Preference — In the event of liquidation, dissolution, or winding-up of Acusphere, and before any distribution to common stockholders and any prior series of preferred stock, the holders of Series A, B, C, D, E, F, I, J and J-1 Preferred Stock are entitled to receive $1.00, $1.60, $2.14, $3.00, $3.30, $4.75, $4.75, $1.41, and $1.41 per share, respectively, plus all accrued but unpaid dividends.

Conversion **—** Shares of preferred stock are convertible, at the option of the holders, in total or in part, into the following number of shares of common stock, subject to future adjustments for dilutive issuances of stock, if any:

Series of Preferred Stock	Number of Shares of Preferred Stock	Conversion Ratio	Equivalent Shares of Common Stock
Series A	565,810	0.17	94,302
Series B	1,544,426	0.17	265,708
Series C	3,481,939	0.18	640,150
Series D	3,238,442	0.19	630,047
Series E	649,299	0.20	127,998
Series F	4,932,724	0.21	1,014,305
Series I	1,354,500	0.56	760,505
Series J	10,736,960	0.17	1,789,493
Series J-1	4,640,983	0.33	1,546,994
Total	31,145,083		6,869,502

Outstanding warrants and options to purchase shares of the Company, the origination of which are described in Notes 5 and 10, convert into common stock based upon the same ratios as follows:

Series of Preferred Stock	Exercise Price Per Share	Number of Shares of Preferred Stock	Equivalent Shares of Common Stock
Series A	$ —	—	—
Series B	1.60	50,000	8,601
Series C	2.14	66,589	12,241
Series D	3.00 - 3.30	93,258	19,616
Series E	3.30 - 4.29	439,045	107,227
Series F	4.75	312,106	64,176
Series I	—	—	—
Series J	—	—	—
Series J-1	—	—	—
Total		960,998	211,861

The preferred stock is automatically converted into common stock at any time upon the vote of fifty-five percent (55%) or more of the then outstanding shares of voting preferred stock, voting together as a single class with each share of preferred stock having one vote for each share of common stock into which it could then convert, except Series J-1 which votes a lesser relative number of shares, as defined.

The preferred stock is automatically converted into common stock upon the consummation of an initial public offering of Acusphere's common stock in which the common stock is sold for a minimum per share and gross proceeds amount, as follows:

Series of Preferred Stock	Minimum Per-Share Amount	Minimum Gross Proceeds
Series A and B	$5.00	$10,000,000
Series C	6.42	10,000,000
Series D	9.00	15,000,000
Series E, F, and I	9.90	15,000,000
Series J and J-1	2.82	30,000,000

Redemption — The holders of the Series A, B, C, D, E, F, I, J, and J-1 Preferred Stock, upon approval of at least 66⅔% of the voting power of all the outstanding shares, voting as a single class, may require that Acusphere redeem all, but not less than all, of their shares beginning at any time after April 25, 2005. If so elected, the redemption price for each share of preferred stock is the original price paid for such stock as adjusted for stock splits, stock dividends, or other recapitalizations, plus all unpaid dividends.

9. Research and License Agreements

Acusphere has clinical and pre-clinical study research agreements with various institutions. Acusphere has incurred expenses in an aggregate of approximately $2,763,000, $2,761,000 and $1,350,000 in sponsored-research expenses relating to such agreements during the years ended December 31, 2000, 2001 and 2002, respectively.

10. Commitments

Operating Leases — Acusphere has leased office and laboratory space under various agreements classified as operating leases. During 2000, 2001, and 2002, rent expense totaled approximately $681,000, $1,349,000, and $2,601,000, respectively.

In March 2001, Acusphere entered into a 10-year lease for a new facility which began in December 2001. As part of the lease agreement, Acusphere is required to maintain a security deposit totaling $997,500 as a condition of this lease. This amount is included in other assets at December 31, 2001 and 2002. In conjunction with the lease agreement, Acusphere issued a warrant to the lessor to purchase 150,000 shares of Series F Nonvoting Redeemable Convertible Preferred Stock. Acusphere recorded the deemed fair value of the warrant of $536,402 as a deferred rent expense included in other assets, which is being amortized over the lease term as rent expense, based upon the Black-Scholes option-pricing model.

Future minimum payments due under the noncancelable facility lease are as follows as of December 31, 2002:

Year Ending December 31,	
2003	$ 2,065,000
2004	2,137,000
2005	2,212,000
2006	2,289,000
2007	2,369,000
Thereafter	10,337,000
	$21,409,000

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.

12. Quarterly Financial Data and Revision of 2003 Stock-Based Compensation (Unaudited)

The following table presents unaudited quarterly financial data of the Company. The Company's quarterly results of operations for these periods are not necessarily indicative of future results of operations.

	Net Loss	Net Loss Available to Common Stockholders	Net Loss Available to Common Stockholders Per Share — Basic and Diluted
Year Ended December 31, 2001			
First Quarter	$(3,503,999)	$ (4,995,776)	$(10.62)
Second Quarter	(4,278,526)	(5,790,159)	(12.00)
Third Quarter	(3,972,424)	(5,584,409)	(11.52)
Fourth Quarter	(6,522,243)	(8,155,464)	(16.56)
Year Ended December 31, 2002			
First Quarter	(6,353,618)	(7,986,375)	(16.14)
Second Quarter	(5,420,147)	(7,071,476)	(14.16)
Third Quarter	(5,701,435)	(7,401,784)	(7.20)
Fourth Quarter	(4,421,050)	(6,102,093)	(5.10)
Year Ended December 31, 2003			
First Quarter	(4,488,190)	(6,097,357)	(5.05)
Second Quarter	(5,418,451)	(7,044,229)	(5.83)

Subsequent to the Company's filing of its Registration Statement on Form S-1, as amended in August 2003, the Company revised the estimated fair value of certain restricted stock and stock option grants. These changes in estimates resulted in additional stock-based compensation expense of $269,000 for the six months ended June 30, 2003. Additionally, the Company recorded $1.4 million of additional deferred

stock-based compensation with a corresponding increase in additional paid-in capital. The Company's 2003 unaudited consolidated financial statements have been revised to reflect this non-cash adjustment. See Notes 2 and 9 for discussion of the Company's accounting for stock options and use of estimates in conjunction with calculating stock-based compensation.

13. Subsequent Event

On April 11, 2003, the Company issued secured subordinated convertible promissory notes to existing investors in exchange for $19,100,000. The notes bear interest at a rate of 10% per annum. The notes and accrued interest will automatically convert into equity upon the occurrence of certain events, including a sale of additional private equity of at least $10,000,000 or a public offering of the Company's stock with a majority vote of the holders of the notes. The type and price of the conversion is either an equity security identical to the Series J at a per share purchase price of $1.41 or the type of equity security issued in the next private equity financing of the Company at a per share purchase price not to exceed $2.12. If not converted to equity, the notes are due June 30, 2004. In addition, the Company issued warrants to each of the note holders to purchase an amount of the Company's stock equal to 20% of the principal amount of the notes with the type of stock issued for the warrants being identical to the Series J or the type of equity security issued in the next private equity financing of the Company. The exercise price of the warrants is to be the original issuance price of the related shares, subject to adjustment under defined circumstances. Based on the relative value of the notes and the deemed value of the warrants, the Company allocated $761,500 (unaudited) of the proceeds to the warrants. The carrying value of the notes is reduced by the unamortized discount. The Company is amortizing this discount through the maturity date of the notes. In conjunction with this issuance of notes, the Company increased the number of shares of stock authorized and reserved for issuance.

On July 1, 2003, the Company filed a registration statement with the Securities and Exchange Commission for the proposed sale of shares of the Company's common stock. 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.

* * * * * *

INDEPENDENT AUDITORS' REPORT

To the Board of Directors and Shareholders of
Acusphere Newco, Ltd.
Hamilton, Bermuda

We have audited the accompanying balance sheets of Acusphere Newco, Ltd. (a development stage company) (the "Company") as of December 31, 2001 and 2000, and the related statements of operations, stockholders' deficit, and cash flows for the year ended December 31, 2001, and for the period from inception (June 28, 2000) to December 31, 2000 and for the period from inception (June 28, 2000) to December 31, 2001. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, such financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2001 and 2000, and the results of its operations and its cash flows for the year ended December 31, 2001, and for the period from inception (June 28, 2000) to December 31, 2000, and for the period from inception (June 28, 2000) to December 31, 2001, in conformity with accounting principles generally accepted in the United States of America.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. The Company is a development stage enterprise engaged in developing, testing, registration, manufacturing, commercialization and licensing of pulmonary drug delivery product candidates. As discussed in Note 1 to the financial statements, the Company's operating losses since inception raise substantial doubt about its ability to continue as a going concern. Management's plans concerning these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of these uncertainties.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
August 9, 2002, except for Note 7, as to
which the date is July 1, 2003

ACUSPHERE NEWCO, LTD.
(A Development Stage Company)

BALANCE SHEETS
DECEMBER 31, 2000 AND 2001

	2000	2001
ASSETS		
CURRENT ASSETS:		
Due from Acusphere (Note 5)	$ —	$ 1,965,840
Due from Elan (Note 5)	—	488,392
Total current assets	$ —	$ 2,454,232
LIABILITIES AND STOCKHOLDERS' DEFICIT		
CURRENT LIABILITIES:		
Due to Acusphere (Note 5)	$ —	$ 2,371,572
Due to Elan (Note 5)	—	82,660
Total current liabilities	—	2,454,232
STOCKHOLDERS' DEFICIT:		
Convertible preferred stock, $1.00 par value; authorized, issued and outstanding, 6,000 shares as of December 31, 2000 and 2001 (liquidation value of $10,485,000)	10,485,000	10,485,000
Common stock, $1.00 par value; authorized, issued and outstanding, 6,000 shares as of December 31, 2000 and 2001	6,000	6,000
Additional paid-in capital	4,509,000	6,963,232
Deficit accumulated during the development stage	(15,000,000)	(17,454,232)
Total stockholders' deficit	—	—
TOTAL LIABILITIES AND STOCKHOLDERS' DEFICIT	$ —	$ 2,454,232

See notes to financial statements.

ACUSPHERE NEWCO, LTD.
(A Development Stage Company)

STATEMENTS OF OPERATIONS

	Period From Inception (June 28, 2000) to December 31, 2000	Year Ended December 31, 2001	Period From Inception (June 28, 2000) to December 31, 2001
OPERATING EXPENSES:			
In-process research and development acquired	$ 15,000,000	$ —	$ 15,000,000
Research and development	—	2,419,736	2,419,736
General and administrative	—	34,496	34,496
NET LOSS	$(15,000,000)	$(2,454,232)	$(17,454,232)

See notes to financial statements.

ACUSPHERE NEWCO, LTD.
(A Development Stage Company)

STATEMENTS OF STOCKHOLDERS' DEFICIT
PERIOD FROM INCEPTION (JUNE 28, 2000) TO DECEMBER 31, 2000 AND YEAR ENDED DECEMBER 31, 2001

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Deficit Accumulated During the Development Stage	Total Stockholders' Deficit
	Number of Shares	Carrying Value	Number of Shares	$1.00 Par Value			
Incorporation of Company:							
Sale of convertible preferred stock	6,000	$10,485,000	—	$ —	$ —	$ —	$ 10,485,000
Sale of common stock	—	—	6,000	6,000	4,509,000	—	4,515,000
Net loss	—	—	—	—	—	(15,000,000)	(15,000,000)
BALANCE, DECEMBER 31, 2000	6,000	10,485,000	6,000	6,000	4,509,000	(15,000,000)	—
Capital contribution	—	—	—	—	2,454,232	—	2,454,232
Net loss	—	—	—	—	—	(2,454,232)	(2,454,232)
BALANCE, DECEMBER 31, 2001	6,000	$10,485,000	6,000	$6,000	$6,963,232	$(17,454,232)	$ —

See notes to financial statements.

ACUSPHERE NEWCO, LTD.
(A Development Stage Company)

STATEMENTS OF CASH FLOWS

	Period From Inception (June 28, 2000) to December 31, 2000	Year Ended December 31, 2001	Period From Inception (June 28, 2000) to December 31, 2001
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$(15,000,000)	$(2,454,232)	$(17,454,232)
Adjustments to reconcile net loss to net cash used in operating activities — changes in operating assets and liabilities:			
Due to Acusphere	—	2,371,572	2,371,572
Due to Elan	—	82,660	82,660
Net cash used in operating activities	(15,000,000)	—	(15,000,000)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Net proceeds from sale of convertible preferred stock	10,485,000	—	10,485,000
Net proceeds from sale of common stock	4,515,000	—	4,515,000
Net cash provided by financing activities	15,000,000	—	15,000,000
NET CHANGE IN CASH	—	—	—
CASH, BEGINNING OF PERIOD	—	—	—
CASH, END OF PERIOD	$ —	$ —	$ —
SUPPLEMENTAL SCHEDULE OF NONCASH FINANCING TRANSACTIONS — Capital contribution due from stockholders	$ —	$ 2,454,232	$ 2,454,232

See notes to financial statements.

ACUSPHERE NEWCO, LTD.
(A Development Stage Company)

NOTES TO FINANCIAL STATEMENTS

1. Operations

On June 28, 2000, Acusphere, Inc. (“Acusphere”) and Elan Corporation, plc and some of its affiliates (“Elan”) formed Acusphere Newco, Ltd. (“Acusphere Newco” or the “Company”) in Bermuda. Acusphere Newco is owned by Acusphere and Elan holding 80.1% and 19.9% (nonvoting shares) interests, respectively. The primary objective of Acusphere Newco is the business of development, testing, registration, manufacturing, commercialization and licensing of pulmonary drug delivery product candidates as defined in the Subscription, Joint Development and Operating Agreement dated June 30, 2000 between Elan and Acusphere.

On June 30, 2000, Elan purchased 1,232,308 shares of Acusphere’s Series G convertible exchangeable preferred stock (“Series G Preferred Stock”) for proceeds of $12,015,003. The Series G Preferred Stock is convertible, at Elan’s option, into Acusphere’s common stock or exchangeable into shares representing a 30.1% interest in Acusphere Newco on a fully diluted basis. Upon the closing of an initial public offering of Acusphere’s common stock, the Series G Preferred Stock automatically converts into Acusphere common stock, which is also exchangeable, at Elan’s option into shares representing a 30.1% interest in Acusphere Newco on a fully diluted basis. Such exchange would increase Elan’s ownership in Acusphere Newco to 50% on a fully diluted basis. Acusphere used the proceeds of the Series G Preferred Stock sale to purchase its 80.1% interest in Acusphere Newco on a fully diluted basis. Acusphere Newco used these proceeds, along with proceeds from Elan’s 19.9% investment, to pay $15.0 million to Elan for a license giving the joint venture rights to use Elan drug delivery technologies. Immediately upon completing this transaction, the cost of the license was expensed as a research and development cost, as the technology acquired had not yet reached technological feasibility and there was no future alternative use for the technology.

While Acusphere owns 100% of the voting common shares, Elan has retained significant minority investor rights that are considered “participating rights” as defined in Emerging Issues Task Force Issue 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 overcome the presumption that Acusphere exercises control over Acusphere Newco.

Upon continued agreement of a business plan, and once agreement has been reached on funding, Acusphere and Elan may contribute to Acusphere Newco in relation to their relative ownership interests (see Note 5). In June 2000, Acusphere entered into a $8,010,000 subordinated note agreement (the “Note Agreement”) with Elan. The borrowings under the Note Agreement are restricted for Acusphere’s funding of Acusphere Newco. As of December 31, 2000 and 2001, there were no borrowings outstanding under the Note Agreement and as of December 31, 2001 there has not been an agreement for additional funding by Elan.

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

The accompanying financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. As shown in the financial statements, the Company has incurred a cumulative net loss of approximately $17.4 million since inception. In addition, and as discussed in Note 6, Elan and Acusphere have

commenced negotiations to terminate their joint venture agreement which may result in the termination of future finding of the Company.

The financial statements do not include any adjustments relating to the recoverability and classification of asset carrying amounts or the amounts and classifications of liabilities that might be necessary should the Company be unable to continue as a going concern.

2. Summary of Significant Accounting Policies

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

Fair Value of Financial Instruments — The carrying amounts of Acusphere Newco's financial instruments, which include the amounts due from stockholders and the amounts due to Acusphere and Elan, approximate their fair value due to their short-term nature.

Concentrations of Limited Suppliers — Certain materials used in Acusphere Newco's development process are procured from a single source. The failure of a supplier, including a subcontractor, to deliver on schedule could delay or interrupt the development process and thereby adversely affect Acusphere Newco's operating results.

Use of Estimates — The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the 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 estimates.

Research and Development Expenses — Acusphere Newco charges research and development expenses to operations as incurred.

Comprehensive Loss — Comprehensive loss is defined as the change in stockholders' equity during a period from transactions and other events and circumstances from nonowner sources. Acusphere Newco's net loss is equal to its comprehensive loss for all periods presented.

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 Newco has viewed its operations and manages its business as principally one operating segment.

Recently Issued Accounting Pronouncements — In August 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets." This statement supersedes SFAS No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," and the accounting and reporting provisions of Accounting Principles Board Opinion No. 30, "Reporting the Results of Operations — Reporting the Effects of Disposal of a Segment of a Business, and Extraordinary, Unusual and Infrequently Occurring Events and Transactions." Under this statement it is required that one accounting model be used for long-lived assets to be disposed of by sale, whether previously held and used or newly acquired, and it broadens the presentation of discontinued operations to include more disposal transactions. The provisions of this statement are effective for financial statements issued for fiscal years beginning after December 15, 2001, and interim periods within those fiscal years, with early adoption permitted. The Company is currently evaluating the ultimate impact of this statement on its results of operations or financial position until such time as its provisions are applied.

3. Income Taxes

Under current Bermuda law, Acusphere Newco is not required to pay any taxes in Bermuda on either income or capital gains. Acusphere Newco has received an undertaking from the Minister of Finance in Bermuda that, in the event of such taxes being imposed, Acusphere Newco will be exempted from taxation until the year 2016.

4. Stockholders' Deficit

Authorized Stock — Acusphere Newco has authorized capital stock of 12,000 shares, of which 6,000 are $1.00 par value common stock and 6,000 are $1.00 par value convertible preferred stock.

Common Stock — In June 2000, Acusphere Newco sold 6,000 shares of common stock resulting in net proceeds of $4,515,000.

Convertible Preferred Stock — In June 2000, Acusphere Newco sold 6,000 shares of convertible preferred stock ("Preferred Stock") resulting in net proceeds of $10,485,000. The rights, preferences and privileges of the Preferred Stock are as follows:

Voting Rights — Preferred stockholders do not have voting rights.

Dividends — Preferred stockholders are entitled to dividends as and when declared by the board of directors. Preferred stockholders are entitled to participate equally on a pro rata basis in any dividend declared for the holders of common stock.

Liquidation Preference — In the event of liquidation, dissolution or winding-up of Acusphere Newco and before any distribution to common stockholders and any prior series of preferred stock, the holders of Preferred Stock are entitled to receive $1,250 per share, respectively, plus all declared but unpaid dividends.

Conversion — Each share of Preferred Stock is convertible, at the option of the holder, into one share of common stock, subject to adjustments for dilutive issuances of stock at any time after June 30, 2002.

5. Related-Party Transactions

Acusphere Newco's research and development and general and administrative costs were paid for directly by the Acusphere Newco stockholders. These transactions are in the normal course of operations and amounts payable to their stockholders are summarized as follows:

The following table summarizes Acusphere Newco's related-party transactions:

	2000	2001
Due to Acusphere	$ —	$2,371,572
Due to Elan	—	82,660
Total	$ —	$2,454,232

These balances are unsecured and interest-free with no set terms of repayment. They are classified as current liabilities as Acusphere Newco will reimburse Acusphere and Elan upon its funding by its stockholders.

Due from stockholders represents the amounts required to be funded into Acusphere Newco as contributed capital by its stockholders. As of December 31, 2001, once agreement has been reached on

funding, Acusphere and Elan would be required to contribute $1,965,840 and $488,392, respectively. Acusphere plans to fund its obligation upon the draw down of the Note Agreement (see Note 1).

6. Subsequent Event

In July 2002, Elan and Acusphere commenced negotiations to terminate their joint venture agreement. These negotiations may result in the assignment to Acusphere of development rights to any project undertaken by the joint venture since its formation in exchange for participation in certain revenues that may be realized in the future.

7. Termination and Dissolution of Joint Venture

In September 2002, Elan and Acusphere terminated the joint venture, at which time Acusphere Newco became a wholly-owned subsidiary of Acusphere. In February 2003, Acusphere Newco was dissolved by Acusphere.

* * * * * *

3,750,000 Shares

ACUSPHERE

Common Stock

Prospectus

SG Cowen
Thomas Weisel Partners LLC
U.S. Bancorp Piper Jaffray
Friedman Billings Ramsey

October 7, 2003