SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2001

OR

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

For the transition period from _____ to _____

Commission File Number 0-30739

INSMED INCORPORATED

(Exact name of registrant as specified in its charter)

Virginia	**54-1972729**
(State or other Jurisdiction of incorporation or organization)	**(I.R.S. employer identification no.)**
4851 Lake Brook Drive **Glen Allen, Virginia 23060**	**(804) 565-3000**
(Address of principal executive offices) (zip code)	**(Registrant's telephone number including area code)**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
None	**None**

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

(Title of class)
Common Stock

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

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

The aggregate market value on February 28, 2002, of the voting stock held by non-affiliates of the registrant was $70,551,251 (based on the closing price for shares of the registrant's Common Stock as reported on the Nasdaq National Market on that date). In determining this figure, the registrant has assumed that all of its directors, officers and persons owning 10% or more of the outstanding Common Stock are affiliates. This assumption shall not be deemed conclusive for any other purpose.

As of February 28, 2002, there were 32,951,644 shares of the registrant's Common Stock, $.01 par value, outstanding.

Portions of the registrant's definitive Proxy Statement to be filed with the Securities and Exchange Commission no later than 120 days after the registrant's fiscal year ended December 31, 2001, and to be delivered to shareholders in connection with the 2002 Annual Meeting of Shareholders, are incorporated in Part III by reference.

INSMED INCORPORATED

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In this Form 10-K, the "Company," "Insmed," "Insmed Incorporated," "we," "us" and "our" refer to Insmed Incorporated, a Virginia corporation. SomatoKine® is a registered trademark of Insmed. This Form 10-K also contains trademarks of third parties. Each trademark of another company appearing in this Form 10-K is the property of its owner.

PART I

ITEM 1. BUSINESS

Introduction

We discover and develop pharmaceutical products for the treatment of metabolic and endocrine diseases primarily associated with insulin resistance. Insulin resistance is a defect in the body that results in decreased sensitivity to insulin, the principal hormone that regulates glucose levels in the bloodstream. Our lead product candidate, INS-1, is an orally-active insulin sensitizer, which restores tissue sensitivity to insulin. We are developing INS-1 for the treatment of type 2 diabetes and polycystic ovary syndrome, commonly known as PCOS. Our second product candidate, SomatoKine, is a recombinant protein that we are developing as an injectable insulin sensitizer targeted towards the management of both type 1 and type 2 diabetics who are less sensitive to insulin therapy. We believe our product candidates address major clinical needs in the management of the diabetic population.

Medical Background

Insulin Resistance

Insulin resistance is a defect in the body's ability to properly respond to insulin, the principal hormone that regulates glucose levels in the bloodstream. Insulin resistance is an important metabolic disorder that precedes the development of diseases such as type 2 diabetes and PCOS. It is frequently asymptomatic and is thought to exist in approximately 25% of the general population in the United States. Although the exact cause is unclear, genetic and other factors such as obesity and a sedentary lifestyle are contributing factors.

Diabetes

Diabetes is a metabolic disease characterized by an inability to properly store and utilize glucose and is caused by either a deficiency of insulin or insulin resistance. The diabetic population consists of two types. Type 1 diabetes, usually emerging during childhood, comprises between 5% and 10% of the diabetic population and is caused by destruction of the cells of the pancreas that produce insulin. In contrast, type 2 diabetes, which represents between 90% and 95% of diabetes cases, usually emerges during middle age as a result of insulin resistance. The common manifestation of both types of diabetes is a persistent state of abnormally high levels of blood glucose, referred to as hyperglycemia. These sustained elevations in the blood glucose level may cause organ damage and both life-threatening and severely debilitating diseases, including kidney disease, blindness and cardiovascular disease.

According to the American Diabetes Association, diabetes afflicts approximately 16 million Americans and, each year, approximately 800,000 new cases are diagnosed and 200,000 Americans die from diabetes-related complications. An article published in the September 12, 2001 issue of The Journal of the American Medical Association reported that the prevalence of diabetes in U.S. adults increased from 4.9% in 1990 to 7.3% in 2000 and, according to a recent report from the Centers for Disease Control and Prevention, this prevalence should continue to increase due to the increasing rate of obesity. Diabetes is currently the sixth leading cause of death by disease in the United States, the leading cause of blindness in people aged 20 to 74 and the cause of approximately 40% of all new cases of kidney failure. In addition, cardiovascular disease is two to four times more prevalent in diabetics than in non-diabetics. The annual cost for health-related expenditures associated with diabetes is estimated to be about $98 billion in the United States.

Current Therapies for Diabetes

There are few therapeutic options available for treatment of the diabetic patient. The mainstay therapies consist primarily of insulin, particularly in the type 1 diabetic, and oral hypoglycemic drugs for the type 2 diabetic who has failed exercise and dietary modification. According to the American Diabetes Association, 43% of all diabetic patients use insulin, and a similar percentage use oral drugs.

The current marketplace for oral hypoglycemic drugs includes the following: Glucophage®, Glucophage XR®, sulfonylureas and, more recently, Glucovance® and thiazolidinediones such as Avandia® and Actos®. During 2000, the largest selling anti-diabetic drug in the United States was Glucophage, a product marketed by Bristol-Myers Squibb that generated in excess of $1.0 billion in annual sales.

Even though these drugs service a multi-billion dollar market, they have limitations in clinical use:

- Glucophage has been associated with diarrhea, nausea and lactic acidosis.
- Sulfonylureas have been associated with increased cardiovascular mortality and are capable of producing severe hypoglycemia, which is a state of low blood sugar.
- Thiazolidinediones may precipitate weight gain, edema and increases in cardiovascular disease. Rezulin, which was manufactured by Parke-Davis, a division of Warner-Lambert Company (now Pfizer Inc.), and generated approximately $625 million in sales in 1999, was withdrawn from the market on March 22, 2000 after being linked to liver damage.

Polycystic Ovary Syndrome (PCOS)

PCOS is a major women's health disorder that affects an estimated 6% of women of reproductive age in the United States. PCOS is characterized by high levels of testosterone and the absence of ovulation and is the leading cause of female infertility in the United States. Women with this disorder are often overweight, have excess facial and body hair and have menstrual irregularities. According to an April 2000 Practice Committee Report published by the American Society for Reproductive Medicine, clinical studies have demonstrated that excess testosterone concentrations decrease and ovulation resumes when insulin resistance is reduced by either drugs or by diet, suggesting that insulin resistance is one of the primary underlying causes of this disorder. Studies have indicated that women with PCOS have a four-fold increase in the risk of developing hypertension, a seven-fold increase in the risk of developing type 2 diabetes and a seven-fold increase in the risk of having a heart attack. In addition, women with PCOS have a higher risk of developing endometrial cancer.

Current Therapies for PCOS

There are currently no drugs approved to address the underlying cause of PCOS, namely insulin resistance. While there are drugs that have been approved for the treatment of PCOS, these drugs target the symptoms of PCOS rather than directly addressing insulin resistance. Such treatments include various fertility agents and cosmetic approaches to treat excess facial and body hair. In addition, Glucophage, which is indicated for the treatment of type 2 diabetes, is sometimes prescribed, although it is not approved by the Food and Drug Administration (FDA) for the treatment of PCOS.

Our Product Candidates

Completion of clinical trials may take several years or more. The length of time generally varies significantly in accordance with the type, complexity, novelty and intended use of the product candidate.

The following table describes our current drug candidates, their indications and clinical trial statuses.

Product Candidate	Indication	Product Description	Clinical Trial Status
INS-1	Type 2 Diabetes	Oral first line therapy	Phase II
INS-1	PCOS	Oral first line therapy	Phase II
SomatoKine	Type 1 and Type 2 Diabetes	Injectable late stage management	Phase II

INS-1

Our lead product candidate, INS-1, is an orally-active insulin sensitizer. Insulin is the primary hormone that circulates in the bloodstream to regulate blood glucose levels. Insulin, when released from the pancreas, circulates in the bloodstream and binds to receptors located on the outer surface of various organs and tissues, such as the liver, skeletal muscle and fat. After insulin binds to a surface receptor on a normal functioning cell, "insulin mediators" are generated from the cell membrane. These mediators enter the cell and regulate and coordinate the effects of various enzyme systems that control the metabolism and disposal of glucose from the bloodstream. The activation of these enzymes allows for the regulation of blood glucose levels.

We believe that the cell's impaired ability to synthesize these mediators is the primary defect that results in the insulin resistant condition. INS-1 is a naturally-occurring chemical precursor of one of these mediators that we believe acts as a building block to restore mediator formation and enhance insulin sensitivity.

We have a comprehensive, ongoing clinical program for the treatment of both type 2 diabetes and PCOS.

In April 1999, the New England Journal of Medicine published the results of our first completed Phase II clinical trial demonstrating that INS-1 was effective in improving insulin resistance in women with PCOS. This data was obtained from a double-blind single dose placebo-controlled study involving 44 obese women with PCOS. In this study, 22 women received INS-1 and 22 women received placebo. When compared to placebo, INS-1 showed statistically significant reductions in insulin ($p<0.07$) and testosterone concentrations ($p<0.006$) and an improvement in ovulation ($p<0.001$). The study was subsequently extended to explore dose response for a total enrollment of 104 women.

In June 1999, we presented to the American Diabetes Association's annual meeting data from our first completed Phase II clinical trial of INS-1 in type 2 diabetics. This was a multi-center, double-blind placebo-controlled study involving 110 early stage type 2 diabetic patients with 57 patients randomized to receive INS-1 and 53 patients receiving placebo. When compared to placebo, INS-1 showed statistically significant reductions in glucose and lipid levels ($p<0.01$) in subjects that had both abnormally high circulating glucose and lipid concentrations.

In January 2001, we reported that, in patients completing the study protocol who received both INS-1 and a sulfonylurea, there was a statistically significant improvement in glycosylated hemoglobin (HbA1c) of 0.36% compared to those patients receiving a sulfonylurea alone ($p<0.05$). Results from this study are consistent with those reported in previous clinical trials of INS-1. In addition, the improvement in HbA1c was more pronounced (0.80%, $p<0.01$) in those patients who were either better controlled by their sulfonylurea therapy or had a less severe form of their disease as judged by their baseline fasting plasma glucose. The results of this study also

demonstrated that improvement in glycemic control was accompanied by a more favorable lipid profile, thus confirming results from earlier trials.

In February 2001, we announced results of two additional Phase II clinical trials of INS-1: one in obese women with PCOS and one in non-diabetic subjects with dyslipidemia. The trial in obese women with PCOS was a multi-center, double-blind, placebo-controlled, dose range-finding study designed to evaluate the incidence of elevated testosterone and irregular ovulation in women diagnosed with PCOS and the effects of INS-1 in this population. The study involved 223 subjects who received a single, daily oral dose of INS-1 (300mg, 600mg or 1200mg) or placebo for two months. In this population, a statistically significant difference in ovulation rates between the treatment groups was observed (placebo 18%, 300mg 6%, 600mg 32% and 1200mg 44%; $p<0.05$). These results corroborated our previously reported findings. The dyslipidemia trial was an exploratory, double-blind, placebo-controlled study involving 61 subjects who received a single, oral daily dose of 1200 mg of INS-1 for three months. We observed an improvement in lipid profiles after the administration of INS-1 to non-diabetic dyslipidemic subjects. In placebo-treated subjects, LDL cholesterol levels significantly worsened over the course of the study (an increase of 14mg/dL, $p<0.05$), and a trend toward a modest elevation of total cholesterol was observed, although triglyceride levels did not change. In those subjects with elevated LDL cholesterol (>130 mg/dL) at the beginning of the study, treatment with INS-1 caused a significant improvement when compared to placebo (a decrease of 21 mg/dL compared to an increase of 30mg/dL, $p<0.05$) and although there was no change in total cholesterol, a significant reduction from baseline triglyceride levels was observed.

SomatoKine

Our second product candidate, SomatoKine, is indicated for the treatment of patients with type 1 and type 2 diabetes who are less sensitive to insulin therapy. SomatoKine is a therapeutic composition of IGF-1 complexed to a primary binding protein, IGFBP3. In healthy individuals, IGF-1 circulates attached to IGFBP3, which serves to regulate the biological activity of IGF-1. IGF-1 is known to enhance insulin action in patients with diabetes. A number of companies have attempted to boost IGF-1 levels in the human body by delivering IGF-1 without IGFBP3; however, the administration of free IGF-1 has generally been associated with significant side effects that have limited its clinical use. We believe that SomatoKine will enhance insulin action without significant side effects.

In April 2000, the Journal of Clinical Endocrinology & Metabolism published the results of our first completed Phase II clinical trial with SomatoKine for type 1 diabetes. This trial demonstrated that SomatoKine showed a statistically significant improvement in insulin sensitivity in patients with type 1 diabetes with no clinically relevant adverse side effects. This data was based on a double-blind, placebo-controlled study involving 12 patients with type 1 diabetes. Specifically, data from this study revealed that when compared to placebo, average daily insulin requirements were significantly reduced ($p<0.01$), average daily blood glucose levels declined ($p<0.02$) and cholesterol levels declined ($p<0.05$). Published results of previous studies by other companies of IGF-1 administered alone without IGFBP3 indicate that patients frequently reported jaw pain, muscular pain, headache and tissue swelling. There were no reports of clinically relevant side effects in this Phase II trial of SomatoKine.

At the 2001 American Diabetes Association meeting, we reported the data from our second trial of SomatoKine in type 2 diabetes patients. Data from this randomized, double-blind study demonstrated that the drug, delivered via continuous infusion or subcutaneous injection, reduced insulin consumption by a range of between 51% to 83% and fasting blood glucose levels by a range of between 29% to 31% in type 2 diabetics.

In January 2002, we announced positive results from a Phase II dose-ranging trial of SomatoKine in patients with type 2 diabetes. This study was placebo-controlled and double-blinded with an eight-day treatment duration to determine the efficacy, safety and pharmacokinetics of SomatoKine in subjects with type 2 diabetes. Thirty-seven subjects were randomized to receive either placebo or SomatoKine at dose levels between 0.125 mg/kg and 2 mg/kg once daily in the evening. All subjects were on insulin therapy prior to enrollment and continued to

receive appropriate insulin doses during a 4-day run-in period as well as during the treatment period. The data demonstrated that statistically significant improvements in insulin sensitivity and fasting blood glucose occurred with the administration of SomatoKine, with the most pronounced changes achieved with a dose of 2 mg/kg. At this dose a significant decrease in average daily insulin requirement from 70.8 units at baseline to 56.5 units (-20.2%) at the end of the treatment period was observed. Other outcome measurements included the change in fasting blood glucose which was decreased from 171.5mg/dL at baseline to 102.2mg/dL on treatment day eight (-40.4%) for the patient group receiving 2mg/kg of SomatoKine versus a decrease from 151.5mg/dL to 134.8mg/dL (-11%) for the patient group receiving placebo. The study further revealed a dose-dependent occurrence of mild hypoglycemia, which suggests that patients on SomatoKine therapy could have further lowered their daily insulin dose to achieve a desirable fasting blood glucose concentration. We believe the results demonstrated that a single daily dose of SomatoKine can be an effective adjunct to insulin in patients with type 2 diabetes whose blood glucose is poorly controlled by standard insulin regimens.

Business Strategy

We are a product-focused company whose goal is to become the leading biopharmaceutical company treating metabolic and endocrine diseases. The key elements of our strategy are listed below.

Focus on products to treat metabolic and endocrine diseases. We will work to complete the development and approval of our products to treat diabetes and PCOS. We believe these are largely underserved, high-growth markets. Our management team has significant experience in drug development and we will use this expertise to complete our clinical development programs and, if successful, file for regulatory approval in the U.S.

Retain commercial rights to market products in selected markets. We intend to market and distribute INS-1 for the treatment of PCOS in the U.S. through a direct sales force. For our other indications, our goal is to retain marketing rights to our product candidates until the development of the products is essentially complete. We believe this approach will allow us to negotiate optimal terms for any such marketing agreements.

Establish corporate partnerships in target markets. We plan to establish corporate partnerships and other relationships to develop, market and commercialize both INS-1 and SomatoKine for all indications outside the U.S., as well as to market INS-1 for the treatment of type 2 diabetes and to develop and market SomatoKine for the treatment of type 1 and type 2 diabetes.

Outsource manufacturing to deploy resources efficiently. Our management team has significant experience in negotiating and supervising contractual arrangements with third parties for the manufacture of drug products on a cost effective basis. To deploy our resources efficiently, we currently plan to continue to outsource the manufacture of INS-1 and SomatoKine.

Acquire and in-license additional products and technologies. We intend to acquire additional products and technologies that complement our activities within the field of metabolic and endocrine diseases. We believe such acquisitions in fields where we have expertise can be rapidly integrated into our development programs.

Research and Development

We have devoted substantially all of our resources since we began our operations to the research and development of pharmaceutical product candidates for metabolic and endocrine diseases associated with insulin resistance. Our research and development expenses were approximately $35.5 million in 2001, $21.6 million in 2000 and $5.7 million 1999.

Strategic Licensing Agreements

University of Virginia Patent Foundation

Our core technology is based on more than 20 years of insulin resistance research at the University of Virginia. Our license agreement with the University of Virginia Patent Foundation grants a worldwide, exclusive license, including the right to grant sublicenses, to use and practice certain patents related to INS-1 for the treatment of diabetes. The license extends for the full term of the patents. The Foundation may terminate the license upon untimely payment of royalties or our bankruptcy or insolvency. We may terminate the license upon 90 days notice to the Foundation. Either party may terminate upon a material breach by the other party.

In consideration for the license agreement, we are obligated to pay minimum annual licensing fees of $100,000, as well as patent costs through the expiration of the patent rights. We may also have to pay a royalty on net sales of any therapeutic drugs covered by the agreement. Royalties earned by the Foundation will reduce licensing fees and, in the case of patent infringement, we may use up to 50% of royalties otherwise payable to the Foundation to pay expenses we incur to defend the patents.

Taisho Pharmaceutical Co., Ltd.

In July 2000, we entered into an agreement with Taisho Pharmaceutical Co., Ltd. for the development and commercialization of INS-1 in Japan and certain other Asian countries. At that time and in connection with entering into the agreement, Taisho purchased $3 million of our common stock. Under the terms of the agreement Taisho will fund 20% of our development costs outside of Japan and Asia and 100% of our development costs inside of Japan and Asia. Taisho is also obligated to make developmental milestone payments and royalty payments on INS-1 sales in Japan and certain other Asian countries. Taisho, after six months' written notice to Insmed, has the right to terminate the agreement. In addition, either party may terminate the agreement upon material breach or insolvency of the other party, but in the event of our material breach or insolvency, Taisho may continue to research, develop and sell INS-1 pursuant to the agreement.

Patents and Proprietary Rights

Proprietary protection is important to our business, and our policy is to protect our technology by filing patent applications for technology that we consider important. We intend to file additional patent applications, when appropriate, relating to improvements in our technology and other specific products that we develop. As with any pending patent application, there can be no assurance that any of these applications will be issued in the United States or in foreign countries. There also cannot be any assurance that United States or foreign patents issuing from any of these applications will not later be held invalid or unenforceable.

INS-1

We currently possess the rights through ownership or license to eight issued United States patents related to our INS-1 technology, including six issued patents that we have exclusively licensed from the University of Virginia Patent Foundation. We also own seven pending patent applications claiming new medical uses of INS-1 and improved methods to manufacture INS-1 and additional defined compounds. We have filed or intend to file patent applications in many of the major international markets for the majority of these patents and pending patents.

The various issued patents cover use of compounds to treat insulin resistance in type 2 diabetes, reduction of elevated blood sugar in humans, treatment of metabolic diseases characterized by hyperandrogenism and/or anovulation, methods for production of INS-1 and purified insulin mediators and purification processes. The initial terms of these patents expire at various times between May 2009 and January 2018. The patent that claims the use of INS-1 for the treatment of type 2 diabetes expires in 2009. The patent that claims the use of INS-1 for the treatment of PCOS expires in 2018.

SomatoKine

We hold 23 United States issued or allowed patents related to the composition, production, antibodies and methods of use for SomatoKine, including:

- One issued patent and one allowed patent application to IGFBP3 composition-of-matter;

- 11 therapeutic use patents for SomatoKine, IGF-1, IGFBP3 or IGFBP3 fragments for the treatment of various disease conditions, including the use of SomatoKine for the treatment of diabetes; and
- 10 patents regarding novel expression, production or analysis methods, some of which may be used for the manufacture of SomatoKine and pharmaceutical compositions of SomatoKine.

As part of the ongoing development of SomatoKine, we have filed or intend to file patent applications related to new production methods, improved formulations, new medical uses and new dosing regimens in the United States and in many of the major international pharmaceutical markets. The various issued patents related to SomatoKine compositions and methods of production expire in the years 2010 to 2017, and the patent claiming methods to treat diabetes expires in 2019.

We have been granted a European patent with claims to recombinantly produced IGFBP3, therapeutic uses of IGFBP3 and therapeutic uses of SomatoKine. Genentech has opposed the validity of this patent and the date for a hearing at the European Patent Office is pending. We cannot provide any assurance that some or all of our patent claims will not be revoked as a consequence of this opposition.

Third parties, including Genentech, Chiron and Amgen, hold United States patents directed at the production of recombinant IGF-1, IGFBP3 and/or recombinant proteins in general. Many of these patents are expected to expire by 2004. Genentech also holds several United States patents, including one directed to certain DNA molecules encoding IGFBP3, another directed to the IGFBP3 protein and a third directed to production of the IGF-1 protein by certain techniques. In addition, a patent has been issued to Genentech for the co-administration of IGF-1 and IGFBP3 by subcutaneous bolus injection to produce a greater anabolic state. Novartis AG, Beth Israel Hospital and Chiron hold United States patents relating to the use of IGF-1 for the treatment of type 1 diabetes, and Novartis has a United States patent relating to the treatment of osteoporosis with IGF-1. Fujisawa Pharmaceuticals Co., Ltd. has a United States patent that contains claims to methods for treating a specific form of insulin-resistant diabetes using an insulin-like growth factor, and Robert Rieveley holds two issued United States patents relating to combinations of therapeutic agents for treating diabetes. Many of these third party patents also have European counterparts.

We do not expect that we will infringe the third party patents described above. However we can provide no assurance that a third party will not assert a contrary position, and further that such a party will not prevail. If we are found to infringe one or more of these patents, it might have an adverse effect on our ability to conduct our business and prevent us from making, using or selling certain products, including SomatoKine, in the United States. Furthermore, we may not have identified all United States and foreign patents that pose a risk of infringement.

Waxman-Hatch Act

The United States Drug Price Competition and Patent Term Restoration Act of 1984, known as the Waxman-Hatch Act, provides for the return of up to five years of patent term for a patent that covers a new product or its use to compensate for time lost during the regulatory review process. This period is generally one-half the time between the effective date of an investigational new drug application and the submission date of a new drug application (NDA), plus the time between the submission date of a NDA and the approval of that application, subject to a maximum extension of five years. The application for patent term extension is subject to approval by the U.S. Patent and Trademark Office (USPTO), in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension, and there can be no guarantee that the application will be granted. Similar patent term extensions are available under European laws. We intend to apply for such patent term extension(s), where appropriate. However, we cannot provide any assurance that we will receive such patent term extension(s).

The Waxman-Hatch Act also establishes a five-year period of marketing exclusivity from the date of NDA approval for new chemical entities approved after September 24, 1984. In order to obtain this exclusivity, the NDA applicant must submit to the FDA, at the appropriate time, the number and expiration date of any patent which claims the drug that is the subject of the NDA, or which claims a method of using the drug that is the subject of the NDA. Failure to submit this patent information at the appropriate time to the FDA may result in loss of the right to this marketing exclusivity.

During this Waxman-Hatch marketing exclusivity period, no third-party may submit an "abbreviated" NDA or "paper" NDA to the FDA for the same product, using data generated by the NDA holder.

Finally, any abbreviated NDA or paper NDA applicant will be subject to the notification provisions of the Waxman-Hatch Act, which should facilitate our notification about potential infringement of our patent rights. The abbreviated or paper NDA applicant must notify the NDA holder and the owner of any patent applicable to the abbreviated NDA or paper NDA product, of the application and intent to market the drug that is the subject of the NDA.

We intend to apply for such exclusivity, where appropriate. However, we cannot provide any assurance that we will receive such exclusivity for any of our products.

Manufacturing

We currently rely, and plan to continue to rely, on contract manufacturers to produce INS–1 and SomatoKine. Our product candidates will need to be manufactured in a facility by processes that comply with the FDA's good manufacturing practices and other similar regulations. It may take a substantial period of time to begin manufacturing our products in compliance with such regulations. If we are unable to establish and maintain relationships with third parties for manufacturing sufficient quantities of our product candidates and their components that meet our planned time and cost parameters, the development and timing of our clinical trials may be adversely affected.

INS-1

We rely upon contractors for both the supply of raw materials and for manufacturing finished product. We purchase raw materials from more than one commercially established firm. Our necessary raw materials are currently commercially available in quantities far in excess of the scale required to complete all of our future planned Phase II and Phase III clinical trials.

We believe that we have established the methods needed to produce the finished drug product and, although they have not been applied to large scale-up, we believe they will meet our commercial supply requirements. The development of a commercial scale manufacturing process is complex and expensive. We cannot assure you that we will be able to develop this commercial scale manufacturing capability in a timely manner or at all.

We currently purchase both raw materials and finished drug products in accordance with forecast-and-purchase order arrangements, which we expect to replace with long term, semi-exclusive manufacturing agreements.

The bulk drug product is currently produced in the United States under current good manufacturing practices applicable to investigational prescription drugs at two sites — DSM Catalytica Pharmaceuticals Inc. in Greenville, NC and Sigma-Aldrich Fine Chemicals in St. Louis, MO — in facilities registered and subject to inspection by the FDA.

SomatoKine

SomatoKine is a complex of two proteins and is manufactured using recombinant DNA technology. The manufacturing process is complicated and involves expression of the two proteins by bacterial fermentation followed by purification and combination of the two proteins.

To date, we have supplied all of our pre-clinical and clinical Phase II study requirements with SomatoKine previously produced by our subsidiary, Celtrix. Since Celtrix no longer produces SomatoKine, we need to identify a new source for this compound to complete Phase II trials. We have signed a letter of intent with Avecia Limited to develop process improvements needed to manufacture SomatoKine on a larger scale. If these process improvements are successful, we intend to enter into an agreement with Avecia to undertake GMP manufacture of SomatoKine at Avecia's site at Billingham, England. At present, SomatoKine has only been manufactured at Phase II scale; we cannot guarantee that we will be able to produce SomatoKine in the larger scales necessary for Phase III and commercial stages.

Marketing and Sales

We currently have no sales, marketing or distribution capability. In order to commercialize any of our product candidates, we must either internally develop sales, marketing and distribution capabilities or make arrangements with a third party to perform these services.

Our goal is to retain marketing, sales and distribution rights to our product candidates until the development of the products is essentially complete. We believe this approach will allow us to negotiate optimal terms upon commercialization. In international markets, we intend to seek strategic relationships to market, sell and distribute our product candidates.

Competition

We are engaged in an industry that is intensely competitive and characterized by rapid technological progress. In each of our potential product areas, we face significant competition from large pharmaceutical, biotechnology and other companies, as well as universities and research institutions. Most of these companies and institutions have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical trials and obtaining regulatory approvals. In addition, many of these companies have greater experience and expertise in manufacturing and marketing pharmaceutical products.

Since all of our products are under development, we cannot predict the relative competitive position of our products if they are approved for use. However, we expect that the following factors will determine our ability to compete effectively:

- safety and efficacy;
- product price;
- ease of administration; and
- marketing and sales capability.

Diabetes

The primary oral therapies for type 2 diabetes include Glucophage® marketed by Bristol-Myers Squibb, Avandia® marketed by GlaxoSmithKline plc, Actos® marketed by Eli Lilly and Company and Takeda Pharmaceuticals America, Inc. and sulfonylureas marketed by various companies, including Pfizer under the trademark, Glucotrol® XL and Glucotrol®.

Glucophage® XR, a sustained release formulation of Glucophage®, Glucovance®, which is a Glucophage® generic sulfonylurea combination, and generic versions of Glucophage have also been approved to treat type 2 diabetes. We are also aware of other products being developed for the treatment of type 2 diabetes, including but not limited to inhaled and oral insulins, new thiazolidinedione compounds and various hormones.

Insulin is the primary treatment for type 1 diabetes and type 2 diabetes when diet, exercise and oral agents fail.

PCOS

While there are a number of drugs available for the treatment of PCOS, they focus on relief of symptoms rather than the cause of the disease. Such treatments include various fertility agents and cosmetic approaches to treat excess facial and body hair. In addition, drugs, such as Glucophage® which is approved for the treatment of type 2 diabetes but not approved for the treatment of PCOS, are being prescribed for the treatment of PCOS.

Government Regulation

Government authorities in the United States and other countries extensively regulate the research, development, testing, manufacture, promotion, marketing and distribution of drug products. Drugs are subject to rigorous regulation by the FDA in the United States and similar regulatory bodies in other countries. The steps ordinarily required before a new drug may be marketed in the United States are similar to steps required in most other countries and include:

- Pre-clinical laboratory tests, pre-clinical studies in animals and formulation studies and the submission to the FDA of an investigational NDA for a new drug or antibiotic;
- Adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication;
- The submission of a NDA to the FDA; and
- FDA review and approval of the NDA before any commercial sale or shipment of the drug.

Pre-clinical tests include laboratory evaluation of product chemistry and stability, as well as animal studies to evaluate toxicity. The results of pre-clinical testing are submitted to the FDA as part of an investigational NDA. The FDA requires a 30-day waiting period after the filing of each investigational NDA before beginning clinical tests in humans. At any time during this 30-day period or at any time thereafter, the FDA may halt proposed or ongoing clinical trials until the FDA authorizes trials under specified terms. The investigational NDA process may become extremely costly and substantially delay development of our products. Moreover, positive results of pre-clinical tests will not necessarily indicate positive results in clinical trials.

Clinical trials to support NDAs are typically conducted in three sequential phases, but the phases may overlap. During Phase I – the initial introduction of the drug into healthy human subjects or patients – the drug is tested to assess metabolism, pharmacokinetics and pharmacological actions and safety, including side effects associated with increasing doses.

Phase II usually involves studies in a limited patient population to:

- Assess the efficacy of the drug in specific, targeted indications;
- Assess dosage tolerance and optimal dosage; and
- Identify possible adverse effects and safety risks.

If a compound is found to be potentially effective and to have an acceptable safety profile in Phase II evaluations, Phase III trials, also called pivotal studies, are undertaken to further demonstrate clinical efficacy and to further test for safety within an expanded patient population at geographically dispersed clinical study sites.

After completion of the required clinical testing, a NDA is submitted. The FDA may request additional information before accepting a NDA for filing, in which case the application must be resubmitted with the additional information. Once the submission has been accepted for filing, the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA to an appropriate advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by the recommendation of an advisory committee.

If FDA evaluations of the NDA and related manufacturing facilities are favorable, the FDA may issue either an approval letter or an approvable letter. An approvable letter will usually contain a number of conditions that must be met in order to secure final approval of the NDA and authorization of commercial marketing of the drug for certain indications. The FDA may refuse to approve the NDA or issue a not approvable letter, outlining the deficiencies in the submission or the manufacturing site(s) and often requiring additional testing or information.

If regulatory approval of any of our products is granted, it will be limited to certain disease states or conditions. The manufacturers of approved products and their manufacturing facilities will be subject to continual review and periodic inspections. Because we intend to contract with third parties for manufacturing of these products, our control of compliance with FDA requirements will be incomplete. In addition, identification of certain side effects or the occurrence of manufacturing problems after any of its drugs are on the market could cause subsequent withdrawal of approval, reformulation of the drug, additional pre-clinical testing or clinical trials and changes in labeling of the product.

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

Employees

As of December 31, 2001, we had 60 full-time employees. Of these employees, 47 were engaged in research and development and 13 were engaged in general management, finance and administration. None of our employees is covered by any collective bargaining agreement. We consider relations with our employees to be good.

Risk Factors Related to Our Business

Except for the historical information contained in this annual report or incorporated in this annual report by reference, this annual report on Form 10-K and the information incorporated by reference contain forward-looking statements that involve risks and uncertainties. Our actual results may differ materially from those discussed here. Factors that could cause or contribute to differences in our actual results include those discussed in the following section, as well as those discussed in Part II, Item 7 entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this annual report and in any other documents incorporated by reference into this annual report. You should consider carefully the following risk factors, together with all of the other information included in this annual report on Form 10–K. Each of these risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock.

Because our products are in an early stage of development, we have not received regulatory approval for any of our products or released any products for commercial sale; therefore we can give you no assurances that we will succeed in commercializing our products.

Our long-term viability and growth will depend on the successful commercialization of products resulting from our development activities, including INS-1 and SomatoKine. All of our potential products and production technologies are in the research or development stages, and we have generated no revenues from product sales. We will need to conduct significant additional development, laboratory and clinical testing and invest significant additional amounts of capital before we can commercialize our products. We can give you no assurances that we will identify, develop or produce products with commercial potential or that we will secure market acceptance for our products. The failure to commercialize our potential products will adversely affect our business, financial condition and results of operations. In addition, the research, development, testing, clinical trials and acquisition of the necessary regulatory approvals with respect to any given product will take many years and thus delay our receipt of revenues, if any, from any such products. In addition, potential products that appear promising at early stages of development may fail for a number of reasons, including the possibility that the products:

- may be ineffective;
- may cause harmful side effects; or
- may be too expensive to manufacture.

Our products may also fail to receive regulatory approval. In addition, even after regulatory authorities approve our products, the products may fail to achieve market acceptance or the proprietary rights of third parties may prevent their commercialization.

Since we have a limited operating history, a history of operating losses and expect to generate operating losses for the foreseeable future, we may not achieve profitability for some time, if at all.

We are focused on product development and we currently have no sales. Both of our operating subsidiaries have incurred losses each year of their operation and we expect them to continue incurring operating losses for the foreseeable future. The process of developing our products requires significant pre-clinical testing and clinical trials as well as regulatory approvals for commercialization and marketing before we can begin to generate any revenue from product sales. In addition, commercialization of our drug candidates will require us to establish a sales and marketing organization and contractual relationships to enable product manufacturing and other related activity. We expect that these activities, together with our general and administrative expenses, will result in substantial operating losses for the foreseeable future. As of December 31, 2001, our accumulated deficit was $139.8 million. For the year ended December 31, 2001, our consolidated net loss was $37.2 million.

We will need additional funds in the future to continue our operations, but we face uncertainties with respect to our access to capital that could adversely impact our business, financial condition and results of operations.

We will require substantial future capital in order to continue to conduct the time-consuming research and development, clinical studies and regulatory activities necessary to bring our therapeutic products to market and to establish production, marketing and sales capabilities. There can be no assurance that our cash reserves together with any subsequent funding will satisfy our capital requirements. The failure to satisfy our capital requirements will adversely affect our business, financial condition and results of operations. Our future capital requirements will depend on many factors, including the progress of pre-clinical testing and clinical trials, the time and costs involved in obtaining regulatory approvals, the costs involved in filing and prosecuting patent applications and enforcing patent claims and the establishment of strategic alliances and activities required for product commercialization. We believe that existing cash reserves will sufficiently fund our activities through mid-2003.

We may seek additional funding through strategic alliances, private or public sales of our securities or licensing all or a portion of our technology. Such funding may significantly dilute existing shareholders or may limit our rights to our currently developing technology. There can be no assurance, however, that we can obtain additional funding on reasonable terms, or at all. If we cannot obtain adequate funds, we may need to significantly curtail our product development programs and/or relinquish rights to our technologies or product candidates.

If our products fail in clinical trials or if we cannot enroll enough patients to complete our clinical trials, there may be an adverse effect on our business, financial condition and results of operations.

In order to sell our products, we must receive regulatory approval for our products. Before obtaining regulatory approvals for the commercial sale of any of our products under development, we must demonstrate through pre-clinical studies and clinical trials that the product is safe and effective for use in each target indication. Therefore, if our products fail in clinical trials, there will be an adverse effect on our business, financial condition and results of operations. In addition, the results from pre-clinical testing and early clinical trials may not be predictive of results obtained in later clinical trials. There can be no assurance that our clinical trials will demonstrate sufficient safety and effectiveness to obtain regulatory approvals. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in late stage clinical trials even after promising results in early stage development.

The completion rate of our clinical trials is dependent on, among other factors, the patient enrollment rate. Patient enrollment is a function of many factors, including:

- patient population size;
- the nature of the protocol to be used in the trial;
- patient proximity to clinical sites;
- eligibility criteria for the study; and
- competition from other companies' clinical trials for the same patient population.

We believe our planned procedures for enrolling patients are appropriate; however, delays in patient enrollment would increase costs and delay ultimate sales, if any, of our products. Such delays could materially adversely affect our business, financial condition and results of operations.

If we fail to obtain regulatory approvals for our products under development, such failure may adversely affect our business, financial condition and results of operations.

Because our products are in an early stage of development, none has received regulatory approval or been released for commercial sale. The pre-clinical testing and clinical trials of any compounds we develop and the manufacturing and marketing of any drugs produced from such compounds must comply with regulation by numerous federal, state and local governmental authorities in the United States, principally the FDA, and by similar agencies in other countries. No product can receive FDA approval unless human clinical trials show its safety and effectiveness. There can be no assurance that clinical testing will provide evidence of safety and effectiveness in humans or that regulatory agencies will grant approvals for any of our products.

The regulatory process takes many years and requires the expenditure of substantial resources. Data obtained from pre-clinical and clinical activities are subject to varying interpretations that could delay, limit or prevent regulatory agency approval. We may also encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a drug and/or the period required for review of any application for regulatory agency approval of a particular compound. Delays in obtaining regulatory agency approvals could adversely affect the marketing of any drugs that our collaborative partners or we develop. Such delays could impose costly procedures on our collaborative partners' or our activities, diminish any competitive advantages that our collaborative partners or we may attain and adversely affect our ability to receive royalties, any of which could materially adversely affect our business, financial condition and results of operations.

If the FDA grants approval for a drug, such approval may limit the indicated uses for which we may market the drug, and this could limit the potential market for such drug. Furthermore, if we obtain approval for any of our products, the marketing and manufacture of such products remain subject to extensive regulatory requirements. Even if the FDA grants approval, such approval would be subject to continual review, and later discovery of unknown problems could restrict the products future use or cause their withdrawal from the market. Failure to comply with regulatory requirements could, among other things, result in fines, suspension of regulatory approvals, operating restrictions and criminal prosecution. In addition, many countries require regulatory agency approval of pricing and may also require approval for the marketing in such countries of any drug that our collaborative partners or we develop.

We cannot be certain that we will obtain any regulatory approvals in other countries, and the failure to obtain such approvals may materially adversely affect our business, financial condition and results of operations. In order to market our products outside of the United States, our corporate partners and we must comply with numerous and varying regulatory requirements of other countries regarding safety and quality. The approval procedures vary among countries and can involve additional product testing and 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 includes 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.

If our products fail to achieve market acceptance for any reason, such failure may adversely affect our business, financial condition and results of operations.

There can be no assurance that any of our product candidates, if approved for marketing, will achieve market acceptance. If our products do not receive market acceptance for any reason, it will adversely affect our business, financial condition and results of operations. The degree of market acceptance of any products we develop will depend on a number of factors, including:

- the establishment and demonstration in the medical community of the clinical efficacy and safety of our products;
- their potential advantage over existing treatment methods; and
- reimbursement policies of government and third-party payers, including insurance companies.

For example, even if we obtain regulatory approval to sell our products, physicians and healthcare payers could conclude that our products are not safe and effective and physicians could choose not to use them to treat patients. Our competitors may also develop new technologies or products which are more effective or less costly, or that seem more cost-effective than our products. We can give no assurance that physicians, patients, third-party payers or the medical community in general will accept and use any products that we may develop.

We currently have no internal manufacturing or marketing capability, which may make commercializing our products difficult.

We have no internal manufacturing or marketing capability. Failure to successfully manufacture and market our products could materially adversely affect our business, financial condition and results of operations. We intend to enter strategic alliances with other parties that have established commercial scale manufacturing and marketing capabilities. There can be no assurance that we will enter such strategic alliances on terms favorable to us, or at all. If we are unable to establish and maintain relationships with third parties for manufacturing sufficient quantities of our product candidates and their components that meet our planned time and cost parameters, the development and timing of our clinical trials may be adversely affected. In addition, there can be no assurance that an adverse FDA inspection of a contractor's manufacturing facilities would not impede our commercial supply capability. As an alternative, we may choose to commercialize such products on our own, which would require substantial additional funds.

If the FDA or any other regulatory agency permits us to commence commercial sales of 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 marketing and sales force with technical expertise and with supporting distribution capability. Alternatively, we may engage a pharmaceutical company with a large distribution system and a large direct sales force to assist us. There can be no assurance that we will successfully establish sales and distribution capabilities or gain market acceptance for our proprietary 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.

Manufacturing capacity necessary to supply SomatoKine may not be available, which may adversely affect our business, financial condition and results of operations.

The available capacity for the manufacture of recombinant proteins that comprise SomatoKine is limited. A shutdown or disruption in any of these facilities due to technical, regulatory or other problems, resulting in an interruption in supply of these materials, could delay our development activities and adversely impact our business, financial condition and results of operations.

Process improvements in the manufacture of SomatoKine will be necessary to complete Phase II and conduct Phase III clinical trials.

We have signed a letter of intent with Avecia Limited to develop process improvements needed to manufacture SomatoKine on a larger scale. If these process improvements are successful, we intend to enter into an agreement with Avecia to undertake GMP manufacture of SomatoKine at Avecia's site at Billingham, England. At present, SomatoKine has only been manufactured at Phase II scale; we cannot guarantee that we will be able to produce SomatoKine at the larger scales necessary for Phase III and commercial stages. If these process improvements are not successful, our costs will increase and the manufacture of SomatoKine for Phase II and Phase III studies will be delayed. Such delay could materially adversely affect our business, financial condition and results of operations.

If the third-party clinical research organizations we intend to rely on to conduct our future clinical trials do not perform in an acceptable and timely manner, our clinical trials could be delayed or unsuccessful.

We do not have the ability to conduct all facets of our clinical trials independently. We intend to rely on clinical investigators and third-party clinical research organizations to perform a portion of these functions. If we cannot locate acceptable contractors to run a portion of our clinical trials or enter into favorable agreements with them, or if these third parties do not successfully carry out their contractual duties or meet expected deadlines, we will be unable to obtain the required approvals and will be unable to commercialize our product candidates on a timely basis, if at all.

We need collaborative relationships for success.

We currently rely and may in the future rely on a number of significant collaborative relationships for research funding, clinical development and/or sales and marketing. 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 products;
- disputes may arise in the future with respect to the ownership of rights to technology developed with corporate partners;
- disagreements with corporate partners could delay or terminate the research, development or commercialization of product candidates or result in litigation or arbitration;
- contracts with our corporate partners may fail to provide sufficient protection of our intellectual property;
- we may have difficulty enforcing the contracts if one of these partners fails to perform;
- corporate partners have considerable discretion in electing whether to pursue the development of any additional products and may pursue technologies or products either on their own or in collaboration with our competitors; and
- corporate partners with marketing rights may choose to devote fewer resources to the marketing of our products than they do to products of their own development.

Given these risks, a great deal of uncertainty exists regarding the success of our current and future collaborative efforts. Failure of these efforts could delay our product development or impair commercialization of our products.

Uncertainty regarding third-party reimbursement and healthcare cost containment initiatives may negatively affect our business, financial condition and results of operations.

If we succeed in bringing any of our proposed products to the market, we cannot assure you that third parties will consider the products cost-effective or provide reimbursement in whole or in part for their use. Our commercial success will depend in part on third-party payers agreeing to reimburse patients for the costs of products. Government health administration authorities, private health insurers and other organizations generally provide reimbursement. Third-party payers frequently challenge the pricing of new drugs. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Therefore, third-party payers may not approve our products for reimbursement.

If third-party payers do not approve our products for reimbursement, sales will suffer, as some patients will opt for a competing product that is approved for reimbursement. Even if third-party payers make reimbursement available, these payer's reimbursement policies may adversely affect our corporate partners and our ability to sell such 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 reducing 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 such legislative or regulatory proposals, if the government or an agency adopts such proposals, they could materially adversely affect our business, financial condition and results of operations.

Our growth strategy includes acquiring complementary businesses or technologies that may not be available or, if available and purchased or licensed, might not improve our business, financial condition or results of operations.

As part of our business strategy, we expect to pursue acquisitions and in-license new products and technologies. Nonetheless, we cannot assure you that we will identify suitable acquisitions or products or that we can make such acquisitions or enter into such license agreements on acceptable terms. If we acquire businesses, those businesses may require substantial capital, and we cannot assure you that such capital will be available in sufficient amounts or that financing will be available in amounts and on terms that we deem acceptable. Furthermore, the integration of acquired businesses may result in unforeseen difficulties that require a disproportionate amount of management's attention and our other resources. Finally, we cannot assure you that we will achieve productive synergies and efficiencies from these acquisitions.

We intend to conduct proprietary development programs with collaborators, and any conflicts with them could harm our business, financial condition and results of operations.

We intend to enter into collaborative relationships, such as our arrangement with Taisho, which will involve our collaborator conducting proprietary development programs. Any conflict with our collaborators could reduce our ability to obtain future collaboration agreements and negatively influence our relationship with existing collaborators, which could reduce our revenues and have an adverse effect on our business, financial condition and results of operations. Moreover, disagreements with our collaborators could develop over rights to our intellectual property.

Certain of our collaborators could also be or become competitors. Our collaborators could harm our product development efforts by:

- developing competing products;
- precluding us from entering into collaborations with their competitors;
- failing to obtain timely regulatory approvals;
- terminating their agreements with us prematurely; or
- failing to devote sufficient resources to the development and commercialization of products.

If we fail to make payments required under the license agreement with the University of Virginia Patent Foundation, then the Foundation may terminate the license agreement and our rights to the patents licensed to us, which would adversely affect our business, financial condition and results of operations.

We have a license agreement with the University of Virginia Patent Foundation with respect to a number of our patents that obligates us to pay license fees and royalties. We must also pay filing and maintenance costs for the patent rights associated with the license agreement and any new patent applications. If we fail to make payments required under the license agreement, then the Foundation may terminate the license agreement and our rights to the patents licensed to us, which would materially adversely affect our business, financial condition and results of operations.

We face uncertainties related to patents and proprietary technology that may adversely affect our business, financial condition and results of operations.

Our success will depend in part on our ability to:

- obtain patent protection for our products;
- prevent third parties from infringing on our patents; and
- refrain from infringing on the patents of others, both domestically and internationally.

Our patent positions are highly uncertain, and any future patents we receive for our potential products will be subject to this uncertainty, which may adversely affect our business, financial condition and results of operations. We intend to actively pursue patent protection for products arising from our research and development activities that have significant potential commercial value. Nevertheless, it is possible that, in the patent application process, certain claims may be rejected or achieve such limited allowance that the value of the patents would be diminished. Further, there can be no assurance that any patents obtained will afford us adequate protection. In addition, any patents we procure may require cooperation with companies holding related patents. We may have difficulty forming a successful relationship with these other companies.

We can give no assurance that a third party will not claim (with or without merit) that we have infringed or misappropriated their proprietary rights. A variety of third parties have obtained, and are attempting to obtain, patent protection relating to the production and use of IGF-1 and/or IGFBP3. We can give no assurances as to whether any issued patents, or patents that may later issue to third parties, would affect our contemplated commercialization of SomatoKine or INS-1. We can give no assurances that such patent(s) can be avoided, invalidated or licensed. If any third party were to assert a claim for infringement, we can give no assurances that we would be successful in the litigation or that such litigation would not have a material adverse effect on our business, financial condition and results of operation. Furthermore, we may not be able to afford the expense of defending against such a claim.

Third parties, including Genentech, Chiron and Amgen, hold United States patents directed at the production of recombinant IGF-1, IGFBP3 and/or recombinant proteins in general. Many of these patents are expected to expire by 2004. Genentech also holds several United States patents, including one directed to certain DNA molecules encoding IGFBP3, another directed to the IGFBP3 protein and a third directed to production of the IGF-1 protein by certain techniques. In addition, a patent has been issued to Genentech for the co-administration of IGF-1 and IGFBP3 by subcutaneous bolus injection to produce a greater anabolic state. Novartis AG, Beth Israel Hospital and Chiron hold United States patents relating to the use of IGF-1 for the treatment of type 1 diabetes, and Novartis has a United States patent relating to the treatment of osteoporosis with IGF-1. Fujisawa Pharmaceuticals Co., Ltd. has a United States patent that contains claims to methods for treating a specific form of insulin-resistant diabetes using an insulin-like growth factor, and Robert Rieveley holds two issued United States patents relating to combinations of therapeutic agents for treating diabetes. Many of these third party patents also have European counterparts.

We do not expect that we will infringe the third party patents described above. However we can provide no assurance that a third party will not assert a contrary position, and further that such a party will not prevail. If we are found to infringe one or more of these patents, it might have an adverse effect on our ability to conduct our business and prevent us from making, using or selling certain products, including SomatoKine, in the United States. Furthermore, we may not have identified all United States and foreign patents that pose a risk of infringement.

We may have to undertake costly litigation to enforce any patents issued or licensed to us or to determine the scope and validity of another party's proprietary rights. We cannot assure that a court of competent jurisdiction would validate our issued or licensed patents. An adverse outcome in litigation or an interference or other proceeding in a court or patent office could subject us to significant liabilities to other parties, require us to license disputed rights from other parties or require us to cease using such technology, any of which could materially adversely affect our business, financial condition and results of operations.

We have been granted a European patent with claims to recombinantly produced IGFBP3, therapeutic uses of IGFBP3 and therapeutic uses of SomatoKine. Genentech has opposed this patent and the date for a hearing is pending. We cannot provide any assurance that some or all of our patent claims will not be revoked as a consequence of this opposition.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our corporate partners, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Third-party claims that our products infringe on their proprietary rights may adversely affect our business, financial condition and results of operations.

We have entered into license agreements, and may enter into future license agreements, with various licensees to develop and market our products, and we cannot assure that third parties will not claim that we and/or our licensees, by practicing our technology, are infringing on their proprietary rights. If other companies successfully bring legal actions against us or our licensees claiming patent or other intellectual property infringements, in addition to any potential liability for damages, a court could require us and/or our licensees to obtain a license in order to continue to use the affected processes or to manufacture or use the affected products, or alternatively, require us and/or our licensees to cease using such products or processes. Such a result may have an adverse effect on our business, financial condition and results of operations. Any such claim, with or without merit, could result in costly litigation or might require us and/or our licensees to enter into royalty or licensing agreements, all of which could delay or otherwise adversely impact the development of our potential products for commercial use. If a court requires us to obtain licenses, there can be no assurance that we and/or our licensees will be able to obtain them on commercially favorable terms, if at all. Without such licenses, we and/or our licensees may be unable to develop certain products. Our breach of an existing license or our failure to obtain, or our delay in obtaining, a license to any technology that we require to commercialize our products may materially adversely impact our business, financial condition and results of operations.

An inability to compete successfully would harm our business, financial condition and results of operations.

We engage in a business characterized by extensive research efforts, rapid developments and intense competition. We cannot assure 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 crucial factors will include the relative speed with which we can develop products, complete the clinical 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 each of our potential product areas, we face substantial competition from large pharmaceutical, biotechnology and other companies, as well as universities and research

institutions. Relative to us, most of these entities 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 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.

Rapid technological change could make our products obsolete, which could materially adversely affect our business, financial condition and results of operations.

Biotechnology and related pharmaceutical technology have undergone and should continue to experience rapid and significant change. We expect that the technologies associated with biotechnology research and development 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.

We are dependent upon retaining and attracting key personnel and others, the loss of which could materially adversely affect our business, financial condition and results of operations.

We highly depend on the principal members of our scientific and management staff, the loss of whose services might significantly delay or prevent the achievement of research, development or business objectives and would materially adversely affect our business, financial condition and results of operations. Our success depends, in large part, on our ability to attract and retain qualified management, scientific and medical personnel, and on our ability to develop and maintain important relationships with commercial partners, leading research institutions and key distributors. We face intense competition for such personnel and relationships. We cannot assure that we will attract and retain such persons or maintain such relationships.

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.

Our research and development activities involve the use of hazardous materials, which could expose us to damages that could materially adversely affect our business, financial condition and results of operations.

Our research and development activities involve the controlled use of hazardous materials, including hazardous chemicals and radioactive 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, including our insurance coverage. 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. These laws and regulations may require us 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.

We may be subject to product liability claims if our products harm people, and we have only limited product liability insurance.

The manufacture and sale of human therapeutic products involve an inherent risk of product liability claims and associated adverse publicity. We currently have only limited product liability insurance for clinical trials and no commercial product liability insurance. We do not know if we will be able to maintain existing or obtain additional product liability insurance on acceptable terms or with adequate coverage against potential liabilities. This type of insurance is expensive and may not be available on acceptable terms. If we are unable to obtain or maintain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to commercialize our products. A successful product liability claim brought against us in excess of our insurance coverage, if any, may require us to pay substantial amounts. This could have a material adverse effect our business, financial condition and results of operations.

The market price of our stock may continue to be highly volatile.

Our common stock is listed on the Nasdaq National Market under the ticker symbol "INSM." The market price of our stock has been and may continue to be highly volatile, and announcements by us or by third parties may have a significant impact on our stock price. These announcements may include:

- Results of our clinical trials and preclinical studies, or those of our corporate partners or our competitors;
- Our operating results;
- Developments in our relationships with corporate partners;
- Developments affecting our corporate partners;
- Negative regulatory action or regulatory approval with respect to our announcement or our competitors' announcement of new products;
- Government regulations, reimbursement changes and governmental investigations or audits related to us or to our products;
- Developments related to our patents or other proprietary rights or those of our competitors;
- Changes in the position of securities analysts with respect to our stock; and/or
- Operating results below the expectations of public market analysts and investors.

In addition, the stock market has from time to time experienced extreme price and volume fluctuations, which have particularly affected the market prices for emerging biotechnology and biopharmaceutical companies, and which have often been unrelated to their operating performance. These broad market fluctuations may adversely affect the market price of our common stock.

Future sales by existing shareholders may lower the price of our common stock, which could result in losses to our shareholders.

Future sales of substantial amounts of common stock in the public market, or the possibility of such sales occurring, could adversely affect prevailing market prices for our common stock or our future ability to raise capital through an offering of equity securities. Substantially all of our common stock is freely tradable in the public market without restriction under the Securities Act of 1933, unless these shares are held by "affiliates" of our company, as that term is defined in Rule 144 under the Securities Act.

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

We have not thus far paid cash dividends on our common stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our businesses and, therefore, we do not anticipate paying any cash dividends in the foreseeable future.

Certain provisions of Virginia law, our articles of incorporation and our amended and restated bylaws, and our Stockholder Rights Plan make a takeover by a third party difficult.

Certain provisions of Virginia law and our articles of incorporation and amended and restated bylaws could hamper a third party's acquisition of, or discourage a third party from attempting to acquire control of us. The conditions could also limit the price that certain investors might be willing to pay in the future for shares of our common stock. 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 issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of common stock or could adversely affect the rights and powers, including voting rights, of the holders of the common stock. In certain circumstances, such issuance could have the effect of decreasing the market price 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 perhaps discouraging someone from making an acquisition proposal for us;
- the amended and restated bylaws' requirement that shareholders provide advance notice when nominating our directors;
- the inability of shareholders to convene a shareholders' meeting without the Chairman of the Board, the President or a majority of the board of directors first calling the meeting; and
- the application of Virginia law prohibiting us from entering into a business combination with the beneficial owner of 10% or more of our outstanding voting stock for a period of three years after the 10% or greater owner first reached that level of stock ownership, unless we meet certain criteria.

In addition, in May 2001 our board of directors approved the adoption of a Shareholder Rights Plan under which shareholders received rights to purchase new shares of preferred stock if a person or group acquires 15% or more of our common stock. These provisions are intended to discourage acquisitions of 15% or more of our common stock without negotiations with the board. The rights trade with our common stock, unless and until they are separated upon the occurrence of certain future events. Our board of directors may redeem the rights at a price of $0.01 per right prior to the time a person acquires 15% or more of our common stock.

ITEM 2. PROPERTIES

We occupy 46,000 square feet of office and laboratory space in Glen Allen, Virginia. Our annual cost for the space in 2002 is approximately $702,000 under an operating lease that contains annual escalations of 1.75% and expires in October 2006. We believe that our existing facilities are adequate for our current needs and that suitable additional or alternate space will be available on commercially reasonable terms when our lease expires or when we need additional space.

ITEM 3. LEGAL PROCEEDINGS

We are not involved in any legal proceedings that, in our opinion, could have a material adverse effect on our business or financial condition.

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

There were no matters submitted to a vote of our shareholders during the quarter ended December 31, 2001.

PART II

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

Our common stock began trading on The Nasdaq SmallCap Market on June 1, 2000. We moved from The Nasdaq SmallCap Market to the Nasdaq National Market on August 8, 2000. Our trading symbol is "INSM." The following table lists, for the periods indicated, the high and low sale prices per share for our common stock as reported on The Nasdaq SmallCap and Nasdaq National Markets.

	Insmed Common Stock	
Fiscal Year 2001	**High**	**Low**
Fourth Quarter	$ 4.76	$ 2.26
Third Quarter	8.15	2.14
Second Quarter	9.75	3.33
First Quarter	7.00	2.88
Fiscal Year 2000		
Fourth Quarter	16.25	2.56
Third Quarter	19.94	11.00
Second Quarter	18.00	11.00

On February 28, 2002, the last reported sale price for our common stock on the Nasdaq National Market was $2.73 per share. As of February 28, 2002, there were 509 holders of record of our common stock.

We have never declared or paid dividends on our common stock. We anticipate that we will retain all earnings, if any, to support operations and to finance the growth and development of our business. Therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination as to the payment of dividends will be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors our board of directors deems relevant.

ITEM 6. SELECTED FINANCIAL DATA

In the table below, we provide you with selected consolidated financial data. We have prepared this information using the consolidated financial statements of Insmed for the five years ended December 31, 2001. The acquisition of Celtrix closed on May 31, 2000. The purchase method of accounting was used to account for the transaction. Accordingly, the results of operations for Celtrix are included in the historical financial information commencing June 1, 2000. The financial statements for each of the five fiscal years ended December 31, 2001 have been audited by Ernst & Young LLP, our independent auditors.

When you read this selected historical financial data, it is important that you also read the historical financial statements and related notes, as well as "Management's Discussion and Analysis of Financial Condition and Results of Operations" on pages 23 to 26.

	Year Ended December 31,				
	1997	1998	1999	2000	2001
	(in thousands, except per share data)				
Historical Statement of Operations Data:					
Revenues	$ —	$ —	$ —	$ 60	$ 296
Operating expenses:					
Research and development	2,604	3,669	5,657	21,608	35,506
General and administrative	979	1,626	2,189	5,989	4,881
Purchased research and development	—	—	—	50,434	—
Stock compensation	—	—	285	3,564	95
Total operating expenses	3,583	5,295	8,131	81,595	40,482
Operating loss	(3,583)	(5,295)	(8,131)	(81,535)	(40,186)
Interest income, net	103	486	338	1,873	3,017
Loss before income taxes	(3.480)	(4,809)	(7,793)	(79,662)	(37,169)
Income tax expense	—	—	—	200	—
Net loss	$(3,480)	$ (4,809)	$(7,793)	$ (79,862)	($ 37,169)
Basic and diluted net loss per share	$ (1.39)	$ (1.68)	$ (2.47)	$ (4.36)	$ (1.13)
Weighted average shares	2,497	2,868	3,155	18,319	32,871

	December 31,				
	1997	1998	1999	2000	2001
	(in thousands)				
Historical Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 2,050	$11,677	$ 4,635	$ 83,083	$ 51,250
Total assets	2,365	11,938	5,296	102,718	71,606
Stockholders' equity	2,151	11,661	4,462	96,782	59,695

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

The following discussion also should be read in conjunction with the Consolidated Financial Statements and notes thereto.

Overview

We discover and develop pharmaceutical products for the treatment of type 2 diabetes and other metabolic and endocrine disorders associated with insulin resistance. We have two lead drug candidates — INS-1 and SomatoKine — and are actively developing these drugs to treat type 1 and type 2 diabetes and polycystic ovary syndrome (commonly known as PCOS).

We have not been profitable and have accumulated deficits of approximately $139.8 million through December 31, 2001. We expect to incur significant additional losses for at least the next several years until such time as sufficient revenues are generated to offset expenses. In general, our expenditures will increase as development of our product candidates progresses. However, there will be fluctuations from period to period caused by differences in projects required at each stage of development.

The full cost and finalization dates, through commercialization, of our current research and development projects (INS-1 for type 2 diabetes and PCOS; SomatoKine for type 1 and type 2 diabetes) are entirely dependent on the results of our current phase II and potential phase III clinical trials for each project and the subsequent review of these results with the FDA. Therefore, the estimated full cost of completion and the final completion dates for our current research and development projects are unknown at this time.

Results of Operations

Year Ended December 31, 2001 compared to Year Ended December 31, 2000

Research and development expenses consist primarily of costs associated with clinical trials of our product candidates, including the costs of manufacturing, compensation and other expenses related to research and development personnel and facilities expenses.

Prior to the fiscal year ended December 31, 2000, we generally did not track our historical research and development cost by project; rather, we tracked such costs by the type of costs incurred, such as clinical trial costs and manufacturing costs.

For the year ended December 31, 2001, we recorded a net loss of $37.2 million. Research and development expenses increased $13.9 million from $21.6 million in 2000 to $35.5 million in 2001 as a result of increased clinical trial activity. INS-1 expenses increased $9.4 million during 2001, compared to 2000, as follows:

- Amounts paid to contract research organizations and for site grants, monitoring and other clinical trial-related costs increased approximately $10.2 million from $7.6 in 2000 to $17.8 in 2001.
- Contract manufacturing costs to supply INS-1 to our trials decreased $800,000 from $5.0 million in 2000 to $4.2 million in 2001. This decrease was primarily due to timing as we took advantage of extended manufacturing runs in 2000 in order to build inventory for our Phase II trials.

Clinical and contract manufacturing costs related to the development of SomatoKine, the compound we acquired from Celtrix, increased approximately $5.0 million, to $10.0 million in 2001.

General and administrative expenses decreased $1.1 million from $6.0 million for 2000 to $4.9 million for 2001. The decrease is primarily due to higher legal, investor relations and other costs resulting from the acquisition of Celtrix in 2000. Legal fees were also incurred in 2000 to finalize the license agreement with Taisho, transition the SomatoKine patent estate and other general corporate matters, and we incurred fees in 2000 to develop our new web site and other investor materials.

As of December 31, 2001, cash, cash equivalents and marketable securities decreased to $51.3 million from $83.1 million at December 31, 2000. As a result of an increased average cash balance in 2001 compared to 2000, net interest income increased $1.1 million to $3.0 million. The issuance of equity securities produced net proceeds of $251,000 in 2001. Net receivables from Taisho for its portion of certain INS-1 development activities increased $2.3 million to $3.5 million.

Accounts payable and accrued project costs increased $6.0 million from $3.4 million at December 31, 2000 to $9.4 million at December 31, 2001 as a result of increased clinical and manufacturing activity. In addition, we deferred the $2.0 million initial licensing fee paid by Taisho in 2000 as part of the joint development agreement

and are recognizing it as revenue over the life of the related INS-1 patents. Stockholders' equity decreased $37.1 as a result of the net loss in 2001, net of the issuance of equity securities and option exercises. The accumulated deficit at December 31, 2001 increased to approximately $139.8 million due to the Company's 2001 net loss of $37.2 million.

Year Ended December 31, 2000 compared to Year Ended December 31, 1999

For the year ended December 31, 2000, we recorded a net loss of $79.9 million. The largest component of this loss relates to a one-time, non-cash charge of $50.4 million to write off research and development resulting from the purchase of Celtrix in May 2000. The amount of the write-off is based on the value assigned to Celtrix's in-process research and development by an independent third-party appraisal company.

During 2000 we also recognized a $3.6 million non-cash charge for stock compensation. The major component of this non-cash charge related to stock options exercised with a non-recourse note. Generally accepted accounting principles require that compensation be recognized in the financial statements based on the difference between the current market price of the underlying stock and the market price utilized in the previous reporting period. The non-recourse note to which the majority of the charge relates was repaid during 2000; accordingly, we do not anticipate similar charges in future periods.

On July 10, 2000, we signed a definitive agreement with Taisho for the development and commercialization of INS-1 in Japan and other Asian countries. The potential pre-commercialization value of the collaboration is $32 million, which includes license fees and payments for achievement of certain development and regulatory milestones and an equity investment, in March 2000, of $3 million. The collaboration also calls for Taisho to fund a portion of our INS-1 development costs, and we will receive royalties on INS-1 sales in Japan and certain other Asian countries covered by the agreement. Beginning in August 2000, we began to accrete into revenue the initial license fee received from Taisho. The life of the related license agreement is being utilized as the accretion period.

Research and development expenses increased $15.9 million from $5.7 million in 1999 to $21.6 million in 2000 as a result of increased clinical trial activity. INS-1 expenses increased $8.9 million during 2000, compared to 1999, as follows:

- Amounts paid to contract research organizations and for site grants, monitoring and other clinical trial-related costs increased approximately $5.9 million.
- Contract manufacturing costs to supply INS-1 to our trials increased $3.0 million.

We also incurred clinical and contract manufacturing costs of approximately $5.0 million related to the development of SomatoKine, the compound we acquired from Celtrix.

General and administrative expenses increased $3.8 million from $2.2 million for 1999 to $6.0 million for 2000. Salaries and benefits account for the majority of the increase. We increased our general and administrative staff to adapt to our public status and to manage our growing portfolio of intellectual property. Legal fees were also incurred to finalize the license agreement with Taisho, transition the SomatoKine patent estate and other general corporate matters, and we incurred fees to develop our new web site and other investor materials.

As of December 31, 2000, cash, cash equivalents and marketable securities increased to $83.1 million from $4.6 million at December 31, 1999. As a result of the increase in cash balances, net interest income increased $1.5 million to $1.9 million. The issuance of equity securities produced net proceeds of $97.3 million and the acquisition of Celtrix provided net additional cash of $3.6 million. We also recorded net receivables of $1.2 million from Taisho for its portion of certain INS-1 development activities and approximately $16.7 million of goodwill in connection with the Celtrix acquisition.

Accounts payable and accrued project costs increased $2.7 million during 2000 as a result of increased clinical and manufacturing activity and the acquisition of Celtrix, and payroll liabilities increased $500,000 as a result of additional personnel and potential bonus payouts. In addition, we deferred the amount paid by Taisho as an initial license fee and are recognizing it as revenue over the life of the agreement. Stockholders' equity increased $92.3 million as a result of the issuance of equity securities, the acquisition of Celtrix and option exercises. The largest component of the increase in accumulated deficit is the $50.4 million non-cash charge for purchased research and development acquired from Celtrix.

Liquidity and Capital Resources

At December 31, 2001, our cash and cash investments were approximately $51.3 million and were invested in money market instruments and investment grade corporate debt. We believe that our current cash position will be sufficient to fund our operations through mid-2003.

Our business strategy contemplates selling additional equity and entering into agreements with corporate partners to fund research and development, and provide milestone payments, license fees and equity investments to fund operations. We will need to raise substantial additional funds to continue development and commercialization of our products. There can be no assurance that adequate funds will be available when we need them or on favorable terms. If at any time we are unable to obtain sufficient additional funds, we will be required to delay, restrict or eliminate some or all of our research or development programs, dispose of assets or technology or cease operations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We invest excess cash in investment grade, interest-bearing securities and, at December 31, 2001, had $50.5 million invested in money market instruments and investment grade corporate debt. Such investments are subject to interest rate and credit risk. Our policy of investing in highly rated securities whose maturities at December 31, 2001, are all less than one year minimizes such risks. In addition, while a hypothetical 1.0% per annum decrease in market interest rates would reduce interest income in 2002, it would not result in a loss of the principal and the decline in interest income would be deemed immaterial.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by Item 8 is set forth on pages F-1 to F-12.

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

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information presented under the caption "Nominees," "Additional Director Whose Term Expires at the 2003 Annual Meeting (Class III Director)," "Directors Whose Terms Expire at the 2004 Annual Meeting (Class I Directors)" and "Section 16(a) Beneficial Ownership Reporting Compliance" of the Company's definitive Proxy Statement for the 2002 Annual Meeting of Shareholders (the "2002 Proxy Statement") is incorporated herein by reference. Such 2002 Proxy Statement will be filed with the Securities and Exchange Commission in March 2002.

ITEM 11. EXECUTIVE COMPENSATION

The information presented under the captions "Executive Officer Compensation" and "Director Compensation" of the 2002 Proxy Statement is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information presented under the caption "Stock Ownership" of the 2002 Proxy Statement is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information presented under the caption "Certain Relationships and Related Transactions" of the 2002 Proxy Statement is incorporated herein by reference.

PART IV

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

(a) Documents filed as part of this report.

1. FINANCIAL STATEMENTS. The following consolidated financial statements of the Company are set forth herein, beginning on page F-1:

   (i) Report of Ernst & Young LLP, Independent Auditors.

   (ii) Consolidated Balance Sheets.

   (iii) Consolidated Statements of Operations.

   (iv) Consolidated Statement of Stockholders' Equity.

   (v) Consolidated Statements of Cash Flows.

   (vi) Notes to Consolidated Financial Statements.

2. FINANCIAL STATEMENT SCHEDULES.

   None required.

3. EXHIBITS.

   The exhibits that are required to be filed or incorporated by reference herein are listed in the Exhibit Index. Exhibits 10.1 and 10.2 constitute management contracts or compensatory plans or arrangements required to be filed as exhibits hereto.

(b) Reports on Form 8-K.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Richmond, Commonwealth of Virginia, on the 25th day of March, 2002.

INSMED INCORPORATED
a Virginia corporation
(Registrant)

By: /s/ GEOFFREY ALLAN
Geoffrey Allan, Ph.D.
Chairman of the Board, President and Chief Executive Officer (Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities indicated on the 25th day of March, 2002.

Signature	Title
/s/ GEOFFREY ALLAN **Geoffrey Allan, Ph.D.**	Chairman of the Board, President and Chief Executive Officer (Principal Executive Officer)
/s/ KEVIN P. TULLY **Kevin P. Tully**	Treasurer and Controller (Principal Financial and Accounting Officer)
/s/ KENNETH G. CONDON **Kenneth G. Condon**	Director
/s/ GRAHAM K. CROOKE **Graham K. Crooke, MB.BS**	Director
/s/ STEINAR J. ENGELSEN **Steinar J. Engelsen, M.D.**	Director
/s/ EDGAR G. ENGLEMAN **Edgar G. Engleman, M.D.**	Director
/s/ MELVIN SHAROKY **Melvin Sharoky, M.D.**	Director
/s/ RANDALL W. WHITCOMB **Randall W. Whitcomb, M.D.**	Director

REPORT OF INDEPENDENT AUDITORS

The Board of Directors and Stockholders
Insmed Incorporated

We have audited the accompanying consolidated balance sheets of Insmed Incorporated as of December 31, 2001 and 2000 and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Insmed Incorporated at December 31, 2001 and 2000, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

McLean, Virginia
January 16, 2002

INSMED INCORPORATED

CONSOLIDATED BALANCE SHEETS
(in thousands)

	December 31, 2001	2000
ASSETS		
Current assets:		
Cash and cash equivalents	**$ 51,250**	$ 71,628
Marketable securities	**—**	11,455
Due from Taisho Pharmaceutical Co., Ltd.	**3,521**	1,228
Other current assets	**278**	309
Total current assets	**55,049**	84,620
Property and equipment, net	**1,172**	1,628
Goodwill, net	**15,385**	16,220
Other assets	**—**	250
Total assets	**$ 71,606**	$ 102,718
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	**$ 4,427**	$ 2,617
Accrued project costs and other	**4,967**	774
Payroll liabilities	**719**	604
Deferred revenue—current portion	**143**	143
Total current liabilities	**10,256**	4,138
Deferred revenue	**1,655**	1,798
Stockholders' equity:		
Common stock, $.01 par value: authorized shares 500,000,000 in 2001 and 2000; issued and outstanding shares, 32,931,765 in 2001 and 32,797,400 in 2000	**329**	328
Additional capital	**199,177**	198,930
Accumulated deficit	**(139,811)**	(102,642)
Accumulated other comprehensive income	**—**	166
Total stockholders' equity	**59,695**	96,782
Total liabilities and stockholders' equity	**$ 71,606**	$ 102,718

See accompanying notes.

INSMED INCORPORATED

CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Year Ended December 31, 2001	2000	1999
Revenues	**$ 296**	$ 60	$ —
Operating expenses:			
Research and development	**35,506**	21,608	5,657
General and administrative	**4,881**	5,989	2,189
Purchased research and development	**—**	50,434	—
Non-cash stock compensation	**95**	3,564	285
Total operating expenses	**40,482**	81,595	8,131
Operating loss	**(40,186)**	(81,535)	(8,131)
Interest income	**3,017**	1,873	338
Loss before income taxes	**(37,169)**	(79,662)	(7,793)
Income tax expense	**—**	200	—
Net loss	**$(37,169)**	$(79,862)	$(7,793)
Basic and diluted net loss per share	**$ (1.13)**	$ (4.36)	$ (2.47)
Shares used in computing basic and diluted net loss per share	**32,871**	18,319	3,155

See accompanying notes.

INSMED INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
YEARS ENDED DECEMBER 31, 2001, 2000, AND 1999
(in thousands, except share amounts)

	Series A Convertible Participating Preferred Stock	Series B Convertible Preferred Stock	Common Stock	Additional Capital	Notes Receivable from Stock Sales	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
Balance at December 31, 1998	61	36	9	26,589	(47)	(14,987)	—	11,661
Issuance of 47,160 shares of common stock upon exercise of stock options	—	—	1	186	—	—	—	187
Issuance of 3,000 shares of common stock upon exercise of stock warrants	—	—	—	16	(16)	—	—	—
Issuance of 18,750 shares of common stock upon exercise of stock warrants	—	—	—	123	—	—	—	123
Issuance of 2,278 shares of common stock to licensor	—	—	—	11	—	—	—	11
Principal payment on notes receivable	—	—	—	—	2	—	—	2
Accrued interest on notes receivable	—	—	—	—	(3)	—	—	(3)
Recognition of stock compensation expense	—	—	—	285	—	—	—	285
Comprehensive earnings:								
Unrealized loss on marketable securities	—	—	—	—	—	—	(11)	(11)
Net loss	—	—	—	—	—	(7,793)	—	(7,793)
Comprehensive loss	—	—	—	—	—	—	—	(7,804)
Balance at December 31, 1999	61	36	10	27,210	(64)	(22,780)	(11)	4,462
Issuance of 792,298 shares of common stock upon exercise of stock options	—	—	8	906	—	—	—	914
Issuance of 32,500 shares of common stock upon exercise of stock warrants	—	—	—	96	—	—	—	96
Issuance of 93,413 shares of common stock to Taisho Pharmaceuticals Co. Ltd.	—	—	1	2,999	—	—	—	3,000
Issuance of 4,969 shares of common stock to licensor	—	—	—	541	—	—	—	541
Issuance of 1,408,169 shares of common stock and 1,725,330 warrants for cash, net of offering costs of $1,775	—	—	14	32,711	—	—	—	32,725
Issuance of 14,470,553 shares of common stock in connection with the acquisition of Insmed Pharmaceuticals, Inc.	(61)	(36)	145	(48)	—	—	—	—
Issuance of 9,527,385 shares of common stock in connection with the acquisition of Celtrix Pharmaceuticals, Inc.	—	—	95	69,425	—	—	—	69,520
Issuance of 5,500,000 shares of common stock for cash, net of offering costs of $4,746	—	—	55	60,512	—	—	—	60,567
Accrued interest on notes receivable	—	—	—	—	(2)	—	—	(2)
Principal payment on notes receivable	—	—	—	—	66	—	—	66
Recognition of stock compensation expense for employee	—	—	—	3,564	—	—	—	3,564
Recognition of stock compensation expense for consultants	—	—	—	1,014	—	—	—	1,014
Comprehensive earnings:								
Unrealized gain on marketable securities	—	—	—	—	—	—	177	177
Net loss	—	—	—	—	—	(79,862)	—	(79,862)
Comprehensive loss	—	—	—	—	—	—	—	(79,685)
Balance at December 31, 2000	—	—	328	198,930	—	(102,642)	166	96,782
Issuance of 115,962 shares of common stock upon exercise of stock options	—	—	1	93	—	—	—	94
Issuance of 18,403 shares of common stock from Employee Stock Purchase Plan	—	—	—	59	—	—	—	59
Recognition of stock compensation expense for director	—	—	—	95	—	—	—	95
Comprehensive earnings:								
Sale of marketable securities	—	—	—	—	—	—	(166)	(166)
Net loss	—	—	—	—	—	(37,169)	—	(37,169)
Comprehensive loss	—	—	—	—	—	—	—	(37,335)
Balance at December 31, 2001	$—	$—	$329	$199,177	$—	$(139,811)	$ —	$59,695

See accompanying notes.

INSMED INCORPORATED
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31, 2001	2000	1999
Operating activities			
Net loss	**$(37,169)**	$(79,862)	$ (7,793)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	**1,542**	789	87
Gain on sale of property and equipment	**—**	—	1
Gain on sale of marketable securities	**(211)**	—	—
Issuance of stock for services	**—**	1,555	11
Interest accrued on notes receivable from stock sales	**—**	(2)	(3)
Non-cash stock compensation	**95**	3,564	285
Purchased research and development	**—**	50,434	—
Changes in operating assets and liabilities:			
Due from Taisho Pharmaceutical Co., Ltd.	**(2,293)**	(1,228)	—
Other current assets	**31**	(233)	(277)
Other assets	**250**	(250)	—
Accounts payable	**1,810**	850	194
Accrued project costs and other	**4,193**	534	240
Payroll liabilities	**115**	492	22
Deferred revenue	**(143)**	1,941	—
Net cash used in operating activities	**(31,780)**	(21,416)	(7,233)
Investing activities			
Purchases of marketable securities	**—**	(19,224)	(4,330)
Proceeds from marketable securities matured and sold	**11,500**	12,264	—
Purchases of property and equipment	**(251)**	(1,294)	(109)
Acquisition of Celtrix Pharmaceuticals, Inc., net of cash acquired	**—**	3,613	—
Net cash provided by (used in) investing activities	**11,249**	(4,641)	(4,439)
Financing activities			
Proceeds from issuance of common stock	**153**	97,302	312
Repayment of notes receivable from stock sales	**—**	66	—
Net cash provided by financing activities	**153**	97,368	312
Increase (decrease) in cash and cash equivalents	**(20,378)**	71,311	(11,360)
Cash and cash equivalents at beginning of year	**71,628**	317	11,677
Cash and cash equivalents at end of year	**$ 51,250**	$ 71,628	$ 317

See accompanying notes.

1. Description of the Business and Summary of Significant Accounting Policies

Insmed Incorporated (the "Company") discovers and develops pharmaceutical products for the treatment of metabolic and endocrine diseases associated with insulin resistance. Insulin resistance is a defect in the body that results in decreased sensitivity to insulin, the principal hormone that regulates glucose levels in the bloodstream. Insmed's lead product candidate, INS-1, is an orally-active insulin sensitizer, which restores tissue sensitivity to insulin. The Company is developing INS-1 for the treatment of type 2 diabetes and polycystic ovary syndrome, commonly known as PCOS. Its second product candidate, SomatoKine®, is a recombinant protein that is being developed as an injectable insulin sensitizer targeted towards the management of both type 1 and type 2 diabetics who are less sensitive to insulin therapy. The Company believes its product candidates address major clinical needs in the management of the diabetic population.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Insmed Pharmaceuticals, Inc. and Celtrix Pharmaceuticals, Inc. ("Celtrix") All significant intercompany balances and transactions have been eliminated.

Cash and Cash Equivalents

The Company considers investments with maturities of three months or less when purchased to be cash equivalents.

Marketable Securities

Marketable securities consist of corporate debt securities, all of which mature within one year. Management classifies the Company's marketable securities as available-for-sale. Such securities are stated at market value, with the unrealized gains and losses included as a separate component of stockholders' equity. Realized gains and losses and declines in value judged to be other than temporary on securities available for sale, if any, are included in operations. The cost of securities sold is calculated using the specific identification method. As of December 31, 2001 and 2000 the cost basis of marketable securities was $0 and $11,289,000, respectively. The unrealized gain was $0 and $166,000 at December 31, 2001 and 2000, respectively. The realized gain in 2001 was $211,000.

Property and Equipment

Depreciation is provided using the straight-line method over periods ranging from three to seven years. Property and equipment is stated at cost and consists of the following:

	December 31,	
	2001	2000
	(in thousands)	
Research and development equipment	$ 1,799	$1,747
Furniture and office equipment	525	429
	2,324	2,176
Accumulated depreciation	(1,152)	(548)
Property and equipment, net	$ 1,172	$1,628

Goodwill

Goodwill is being amortized on a straight-line basis over twenty years. Accumulated amortization of goodwill was approximately $1,322,000 and $487,000 at December 31, 2001 and 2000, respectively. Management re-evaluates goodwill using undiscounted operating cash flows whenever significant events or changes occur which might impair recovery of recorded costs, and writes down goodwill to its net realizable value, if appropriate.

Fair Value of Financial Instruments

The Company considers the recorded cost of its financial assets and liabilities, which consist primarily of cash and cash equivalents, marketable securities and accounts payable, to approximate the fair value of the respective assets and liabilities at December 31, 2001 due to the short-term maturities of these instruments.

Stock-Based Compensation

The Company recognizes expense for stock-based compensation in accordance with the provisions of Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations. Accordingly, compensation cost is recognized for the excess, if any, of the estimated fair value of the stock at the grant date over the exercise price. Disclosures regarding alternative fair value measurement and recognition methods prescribed by Financial Accounting Standards Board ("FASB") Statement No. 123, *Accounting for Stock-Based Compensation,* are presented in Note 3.

Stock options granted to non-employees are accounted for in accordance with EITF 96-18, Accounting for Equity Instruments that are issued to Other than Employees for Acquiring, or in Conjunction with Selling Goods or Services. Accordingly, the estimated fair value of the equity instrument is recorded on the earlier of the performance commitment date or the date the services required are completed.

Revenue Recognition

Revenue from license agreements is generally recognized over the term of the agreement, or in certain circumstances, when milestones are met. Amounts received for which there is a future performance obligation, are deferred and recognized on a straight-line basis over the life of the agreement.

Income Taxes

Income taxes are accounted for using the liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Net Loss Per Share

Basic net loss per share is computed based upon the weighted average number of common shares outstanding during the year. The Company's diluted net loss per share is the same as its basic net loss per share because all stock options, warrants, and other potentially dilutive securities are antidilutive and, therefore, excluded from the calculation of diluted net loss per share.

Comprehensive Income (Loss)

Under FASB Statement No. 130*, Reporting Comprehensive Income*, the Company is required to display comprehensive loss and its components as part of the consolidated financial statements. Comprehensive loss is comprised of the net loss and other comprehensive income (loss), which includes certain changes in equity that are excluded from the net loss. The Company includes unrealized holding gains and losses on available-for-sale securities in other comprehensive income (loss).

Segment Information

The Company currently operates in one business segment, which is the development and commercialization of pharmaceutical products for the treatment of metabolic and endocrine diseases associated with insulin resistance. The Company is managed and operated as one business. A single management team that reports to the

Chief Executive Officer comprehensively manages the entire business. The Company does not operate separate lines of business with respect to its products or product candidates. Accordingly, the Company does not have separately reportable segments as defined by FASB Statement No. 131, *Disclosure about Segments of an Enterprise and Related Information*.

Reclassifications

Certain prior year amounts have been reclassified to conform to the current year presentation.

Use of Estimates

The preparation of the consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from those estimates.

Recent Accounting Pronouncements

In June 2001, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 141, *Business Combinations* ("SFAS No. 141") and Statement of Financial Accounting Standards No. 142, *Goodwill and Other Intangible Assets* ("SFAS No. 142"). SFAS No. 141 requires that all business combinations be accounted for under the purchase method. SFAS No. 142 will be adopted after December 31, 2001, and requires that an acquired, intangible asset shall initially be recognized and measured based on its fair value. The statement also provides that goodwill shall not be amortized, but shall be periodically tested for impairment by comparing its fair value to its carrying amount. Effective January 1, 2002, amortization of our goodwill will cease, and we will begin performing periodic tests of impairment to comply with the new standard. The Company does not currently anticipate any impact upon adoption of these pronouncements.

2. Acquisition of Celtrix Pharmaceuticals

On May 31, 2000, Insmed Pharmaceuticals, Inc. acquired Celtrix. Celtrix was a biopharmaceutical company focused on developing novel therapeutics for the treatment of seriously debilitating, degenerative conditions primarily associated with severe trauma, chronic diseases or aging. At closing:

- Celtrix and Insmed Pharmaceuticals, Inc. became wholly-owned subsidiaries of the Company.
- Each issued and outstanding preferred and common share of Insmed Pharmaceuticals, Inc. was exchanged for three and one-half shares on a pre-split basis of the Company's common stock.
- Each issued and outstanding common share of Celtrix was exchanged for one share of the Company's common stock.
- The liquidation preference per share ($1,000 per share) plus accrued but unpaid dividends of Celtrix Series A Preferred Stock was convertible into Celtrix common stock at a price per share of $2.006. The holders of Celtrix Series A Preferred Stock received shares of the Company's common stock on an as-converted basis.
- All options and warrants of Insmed Pharmaceuticals, Inc. and Celtrix outstanding at the closing of the transaction converted into options and warrants of the Company.

The purchase method of accounting was used to account for the transaction. The historical basis of Insmed Pharmaceuticals, Inc.'s assets and liabilities carried over to the Company. Approximately 9.5 million shares of the Company's common stock were issued to former Celtrix preferred and common stockholders. Aggregate consideration of $71.7 million, including $2.1 million in transaction costs incurred by Insmed Pharmaceuticals, Inc. was allocated to cash ($5.4 million), equipment and other assets ($427,000), accounts payable ($1.2 million),

in-process research and development ($50.4 million), and goodwill ($16.7 million). The fair value of in-process research and development was determined by an independent third-party valuation.

Aggregate consideration was determined by multiplying the average fair value per share of the Celtrix common stock, for the five days prior to and subsequent to the signing of a definitive agreement on November 30, 1999, by the Celtrix shares outstanding, on an as-converted basis, as of November 30, 1999. The product of this calculation was added to the fair value of options and warrants outstanding at November 30, 1999 and the transaction costs incurred by Insmed Pharmaceuticals. The fair value of options and warrants was determined by using the Black-Scholes pricing method. Pro forma consolidated statements of operations for the years ended December 31, 2000 and 1999 are included below. These statements give effect to the acquisition of Celtrix and related transactions as if such transactions had occurred on January 1, 1999, and include the results of operations for Insmed Incorporated and Celtrix for the periods presented.

	For the Year Ended December 31, 2000	1999
Revenues	$ 188	$ 763
Operating expenses:		
Research and development	22,495	16,492
General and administrative	7,768	4,142
Purchased research and development	50,434	—
Non-cash stock compensation	3,564	285
Total operating expenses	84,261	20,919
Operating loss	(84,073)	(20,156)
Interest income	1,960	423
Other inome	—	600
Loss before income tax expense	(82,113)	(19,133)
Income tax expense	200	—
Net loss	$(82,313)	$(19,133)
Net loss per share–basic and diluted	$ (3.01)	$ (0.77)
Shares used in computing basic and Diluted net loss per share	27,380	24,827

3. Stockholders' Equity

Common Stock

On July 28, 2000, the Company's stockholders approved a one-for-four reverse stock split. The split was effective at the close of business on July 28, 2000, and shares of common stock began trading on the post-split basis at the opening of the Nasdaq stock market on July 31, 2000. Stockholders' equity has been restated to give retroactive recognition to the reverse stock split. In addition, all references in the consolidated financial statements to number of shares and per share amounts have been restated.

On November 1, 2000, the Company sold 6,500,000 shares of common stock at $11.875 per share in a public offering, including 1,000,000 shares that were sold by certain selling shareholders. The proceeds from the sale of 5,500,000 shares approximated $60.6 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

Periodically, the Company has issued shares of common stock in exchange for services provided by stockholders and others. These issuances have been recorded at their estimated fair value at the time of the respective transactions and corresponding amounts have been reflected as expense in the accompanying consolidated statements of operations.

Stock Warrants and Options

On May 31, 2000 Insmed Pharmaceuticals, Inc. issued warrants to purchase 1,725,330 shares of the Company's common stock. The warrants are exercisable for five years at a price of $9.00.

The Company issues stock options to attract and retain executive officers, key employees, non-employee directors and other non-employee advisors and service providers. The current plan provides for issuance of options to purchase up to 3,327,974 shares of common stock, which increases each year by one percent of the number of outstanding shares of common stock on the preceding December 31. The maximum number of shares issuable under the plan is 6,250,000. At December 31, 2001, zero options remain available for new grants. Options may be granted at the discretion of the board of directors, compensation committee or a delegate. The weighted-average fair value of options granted during 2001, 2000, and 1999 was $3.37, $8.23, and $0.38, respectively. A summary of stock option activity is as follows:

Description	2001	Weighted Average Exercise Price	2000	Weighted Average Exercise Price	1999	Weighted Average Exercise Price
Options outstanding at January 1	1,701,735	$7.39	1,490,558	$ 1.06	1,253,722	$1.09
Granted	1,812,465	4.66	1,060,444	11.37	465,924	0.09
Exercised	(115,962)	0.81	(792,298)	1.21	(165,062)	1.13
Cancelled	(254,677)	6.75	(56,969)	4.12	(64,026)	0.43
Options outstanding at December 31	3,143,561	$6.11	1,701,735	$ 7.39	1,490,558	$1.06

The following table summarizes options outstanding at December 31, 2001:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$ 0.172 – $ 0.916	440,872	2.50	$ 0.77	331,422	$ 0.72
$ 1.38 – $ 4.88	1,353,377	6.29	3.98	136,254	4.21
$ 5.000 – $ 8.25	617,985	6.65	6.14	248,125	6.21
$10.000 – $13.063	163,125	7.37	11.65	127,500	11.30
$13.313 – $14.00	565,313	4.62	13.61	141,095	13.61
$32.116	2,889	5.25	32.12	2,889	32.12
	3,143,561	5.58	$ 6.11	987,285	$ 5.89

If the Company had accounted for its employee stock awards under the fair value based method, the net loss would have increased by approximately $2,222,000 for 2001, $627,000 for 2000, and $48,000 for 1999. The basic and diluted net loss per share would have increased $0.07 in 2001, $0.03 in 2000 and $0.01 in 1999. These pro forma amounts are not indicative of future effects of applying the fair value based method since stock-based awards granted may vary from year to year and vesting periods of one to four years were used to measure pro forma compensation expense. The fair value for these awards was estimated at the date of grant using the Black-Scholes pricing method assuming a weighted average volatility of 89% in 2001, 83% in 2000, and 25% in 1999, a risk-free interest rate of 4.5% in 2001, 6% in 2000 and 1999, no dividends, and a weighted-average expected life of the option of 5 years in 2001 and 4 years in 2000 and 1999.

A total of 5,303,304 shares of common stock were reserved at December 31, 2001 in connection with stock options, stock warrants, and the employee stock purchase plan.

4. Income Taxes

The deferred tax assets of approximately $84.5 million and $77 million at December 31, 2001 and 2000, respectively, arise primarily due to net operating loss carryforwards for income tax purposes. Due to the Company's anticipated future losses, these amounts have been entirely offset by a valuation allowance.

At December 31, 2001 and 2000, the Company had net operating loss carryforwards for income tax purposes of approximately $208.4 million and $160.4 million (of which $115 million was acquired from Celtrix), respectively, expiring in various years beginning in 2003. Utilization of these carryforwards will be significantly limited due to changes in the ownership of the Company's common stock.

The Company recognized $200,000 of income tax expense in the year ended December 31, 2000 related to foreign taxes withheld from the initial license fee received from Taisho Pharmaceutical Co., Ltd.

5. Leases

The Company leases office and laboratory space under operating lease agreements expiring in February 2002. The leases provide for monthly rent of approximately $14,300. Since the Company vacated these premises in August 2001, the Company has recognized the applicable January and February 2002 rent expense at December 31, 2001. The Company now leases office and laboratory space under an operating lease agreement expiring in October 2006. The lease provides for monthly rent of approximately $58,000 with a 1.75% escalation per year. The Company also leases a vehicle and office equipment. Future minimum payments on these leases at December 31, 2001 approximate $782,000, $770,000, $762,000, $772,000, and $571,000 in 2002, 2003, 2004, 2005, and 2006, respectively. Rent expense for all operating leases approximated $663,000 in 2001, $319,000 in 2000, and $243,000 in 1999.

6. Employee Benefit Plans

In 2000, the Company adopted a stock purchase plan whereby eligible employees may purchase common stock. Purchases may be made through payroll deductions subject to annual limitations. The purchase price per share under the plan is the lesser of 85% of the fair market value of a share of common stock at the beginning of each offering period or 85% of the fair market value on the date the purchase is made. As of December 31, 2001 there were 250,000 shares authorized for issuance under the plan and 18,403 have been issued.

The Company also maintains a tax-qualified employee savings and retirement plan, (the "401(k) plan") for eligible employees. Participating employees may defer up to the lesser of 25% of W-2 compensation or the maximum amount permitted by the Internal Revenue Code, as amended. The 401(k) plan permits the Company to make matching contributions on behalf of all participants who have elected to make deferrals. To date, the Company has not made any contributions to the plan.

7. License and Collaborative Agreements

Taisho Pharmaceutical Co., Ltd.

In July 2000, the Company entered into an agreement with Taisho Pharmaceutical Co., Ltd. ("Taisho") for the development and commercialization of INS-1 in Japan and certain other Asian countries. The collaboration includes payments upon achievement of certain development and regulatory milestones as well as the receipt of royalties on INS-1 sales in Japan and the other Asian countries covered by the agreement. Taisho will also fund 20% of the development costs for INS-1 in North America and Europe. Development costs reimbursable by Taisho approximated $6.0 million and $2.3 million in 2001 and 2000, respectively, and have been applied to reduce research and development expense. The agreement also provided for an initial license fee of $2.0 million, which has been deferred and is being amortized into revenue, on a straight-line basis, over the estimated life of the agreement. In addition, Taisho purchased 93,413 shares of the Company's common stock in 2000.

UVA Patent Foundation

In 1988, the Company entered into a license agreement with The University of Virginia Alumni Patents Foundation (the "Foundation"). The agreement, as amended, provides the Company with an exclusive, worldwide license to develop and sell products related to certain patent rights for insulin resistance and associated disorders. The Company is obligated to pay minimum annual licensing fees of $100,000, as well as patent costs through the expiration of patent rights. The Company may also have to pay a royalty on net sales of any therapeutic drugs covered by the agreement.

Under the license agreement, the Company was required to issue shares of its common stock each time shares of any class of stock were issued so that the Foundation at all times had a 3% undiluted interest in the Company. The right to receive such stock expired May 31, 2000. Prior to the expiration of this right, the Foundation had received 103,780 shares of common stock under the license agreement. These issuances have been recorded at their estimated fair value at the time of the respective transaction. Related expenses of $641,000 in 2000 and $111,000 in 1999 have been included in research and development expense in the accompanying consolidated statements of operations.

The Company also provided support for research at the University of Virginia ("UVA") that contributes toward commercial development of its planned products. Total expense for research support to UVA amounted to $347,000 in 1999.

8. Quarterly Financial Data (Unaudited)

	Fiscal Quarter							
	First		Second		Third		Fourth	
	2001	2000	2001	2000	2001	2000	2001	2000
	(in thousands, except per share data)							
Revenues	$ 100	$ —	$ 69	$ —	$ 66	$ 53	$ 61	$ 7
Operating Loss	(11,345)	(11,420)	(9,629)	(55,601)	(8,974)	(5,545)	(10,238)	(8,969)
Net Loss	(10,093)	(11,301)	(8,793)	(55,514)	(8,371)	(5,147)	(9,912)	(7,900)
Net Loss Per Share	$ (0.31)	$ (3.26)	$ (0.27)	$ (4.77)	$ (0.25)	$ (0.19)	$(0.30)	$(0.26)

EXHIBIT INDEX

Exhibit Number	Exhibit Title
3.1	Articles of Incorporation of Insmed Incorporated, as amended (previously filed as Annex H to the Joint Proxy Statement/Prospectus contained in Part I of Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
3.2	Amended and Restated Bylaws of Insmed Incorporated (previously filed as Annex I to the Joint Proxy Statement/Prospectus contained in Part I of Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
3.3	Form of Articles of Amendment to Insmed Incorporated's Articles of Incorporation, as amended, creating a new series of Preferred Stock designated as Series A Junior Participating Preferred Stock (previously filed as Exhibit A to the Rights Agreement, dated as of May 16, 2001, between Insmed Incorporated and First Union National Bank, as Rights Agent, filed as Exhibit 4.4 to Insmed Incorporated's Registration Statement on Form 8-A filed with the Securities and Exchange Commission on May, 17, 2001 and incorporated herein by reference).
4.1	Description of Capital Stock (contained in the Articles of Incorporation filed as Exhibit 3.1).
4.2	Specimen stock certificate representing common stock, $.01 par value per share, of the Registrant (previously filed as Exhibit 4.2 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
4.3	Article VI of the Articles of Incorporation of Insmed Incorporated (previously filed as Exhibit 4.1 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
4.4	Rights Agreement, dated as of May 16, 2001, between Insmed Incorporated and First Union National Bank, as Rights Agent (which includes as (i) Exhibit A the form of Articles of Amendment to Insmed Incorporated's Articles of Incorporation, as amended, (ii) Exhibit B the form of Rights Certificate, and (iii) Exhibit C the Summary of the Rights to Purchase Preferred Stock) (previously filed as Exhibit 4.4 to Insmed Incorporated's Registration Statement on Form 8-A filed with the Securities and Exchange Commission on May 17, 2001 and incorporated herein by reference).
4.5	Form of Rights Certificate (previously filed as Exhibit B to the Rights Agreement, dated as of May 16, 2001, between Insmed Incorporated and First Union National Bank, as Rights Agent, filed as Exhibit 4.4 to Insmed Incorporated's Registration Statement on Form 8-A filed with the Securities and Exchange Commission on May 17, 2001 and incorporated herein by reference).
10.1	Insmed Incorporated 2000 Stock Purchase Plan (previously filed as Exhibit 10.1 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.2	Insmed Incorporated 2000 Stock Incentive Plan (previously filed as Exhibit 10.2 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.3	Amended and Restated License Agreement between Insmed Pharmaceuticals, Inc. and the University of Virginia Patent Foundation (previously filed as Exhibit 10.3 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.8+	Subscription, Joint Development and Operating Agreement by and among Celtrix Pharmaceuticals, Inc., Elan Corporation, plc, Elan International Services, Ltd., and Celtrix Newco Ltd. dated as of April 21, 1999 (previously filed as Exhibit 10.8 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).

Exhibit Number	Exhibit Title
10.9+	License Agreement by and between Celtrix Newco Ltd. and Celtrix Pharmaceuticals, Inc. dated as of April 21, 1999 (previously filed as Exhibit 10.9 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.10+	License Agreement by and between Celtrix Newco Ltd. and Elan Pharmaceutical Technologies, a division of Elan Corporation, plc, dated as of April 21, 1999 (previously filed as Exhibit 10.10 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.11	License Agreement, dated as of April 1, 1993, between Genentech, Inc. and Celtrix Pharmaceuticals, Inc. (previously filed as Exhibit 10.11 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.12	Purchase Agreement among Insmed, Inc., Insmed Pharmaceuticals, Inc. and certain investors named therein dated January 13, 2000 (previously filed as Exhibit 10.12 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.13	Form of Warrant of Insmed to be issued pursuant to Purchase Agreement among Insmed Incorporated, Insmed Pharmaceuticals, Inc. and certain investors dated January 13, 2000 (previously filed as Exhibit 10.13 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.14	Form of Registration Rights Agreement among Insmed Incorporated, Insmed Pharmaceuticals, Inc. and certain investors party to the Purchase Agreement among Insmed Incorporated, Insmed Pharmaceuticals, Inc. and certain investors dated January 13, 2000 (previously filed as Exhibit 10.14 to Insmed Incorporated's Registration Statement on Form S-4 (Registration No. 333-30098) and incorporated herein by reference).
10.15+	License Agreement, dated as of July 10, 2000, between Insmed Pharmaceuticals, Inc. and Taisho Pharmaceutical Co., Ltd. (previously filed as Exhibit 10.15 to Insmed Incorporated's Registration Statement on Form S-1 (Registration No. 333-46552) and incorporated herein by reference).
10.16	Sublease, dated March 30, 2001, between Rhodia Inc. and Insmed Incorporated (previously filed as Exhibit 10.15 to Insmed Incorporated's Quarterly Report on Form 10-Q for the quarter ended March 31, 2001 and incorporated herein by reference).
10.17	Consent to Sublease, dated as of April 12, 2001, among A & W Virginia Corporation, as Landlord, Rhodia Inc., as Tenant, and Insmed Incorporated, as Subtenant (previously filed as Exhibit 10.16 to Insmed Incorporated's Quarterly Report on Form 10-Q for the quarter ended March 31, 2001 and incorporated herein by reference).
21.1	Subsidiaries of Insmed Incorporated (previously filed as Exhibit 21.1 to Insmed Incorporated's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated herein by reference).
23.1	Consent of Ernst & Young LLP.

+ The Securities and Exchange Commission has granted confidential treatment with respect to certain information in these exhibits.

EXHIBIT 23.1

Consent of Independent Auditors

We consent to the incorporation by reference in each Registration Statement (Form S-8 Registration Nos. 333-39198 and 333-39200) pertaining to the Insmed Incorporated Employee Stock Purchase Plan and the Insmed Incorporated Stock Incentive Plan, respectively, of our report dated January 16, 2002, with respect to the consolidated financial statements of Insmed Incorporated included in the Annual Report (Form 10-K) for the year ended December 31, 2001.

/s/ Ernst & Young LLP

McLean, Virginia
March 20, 2002