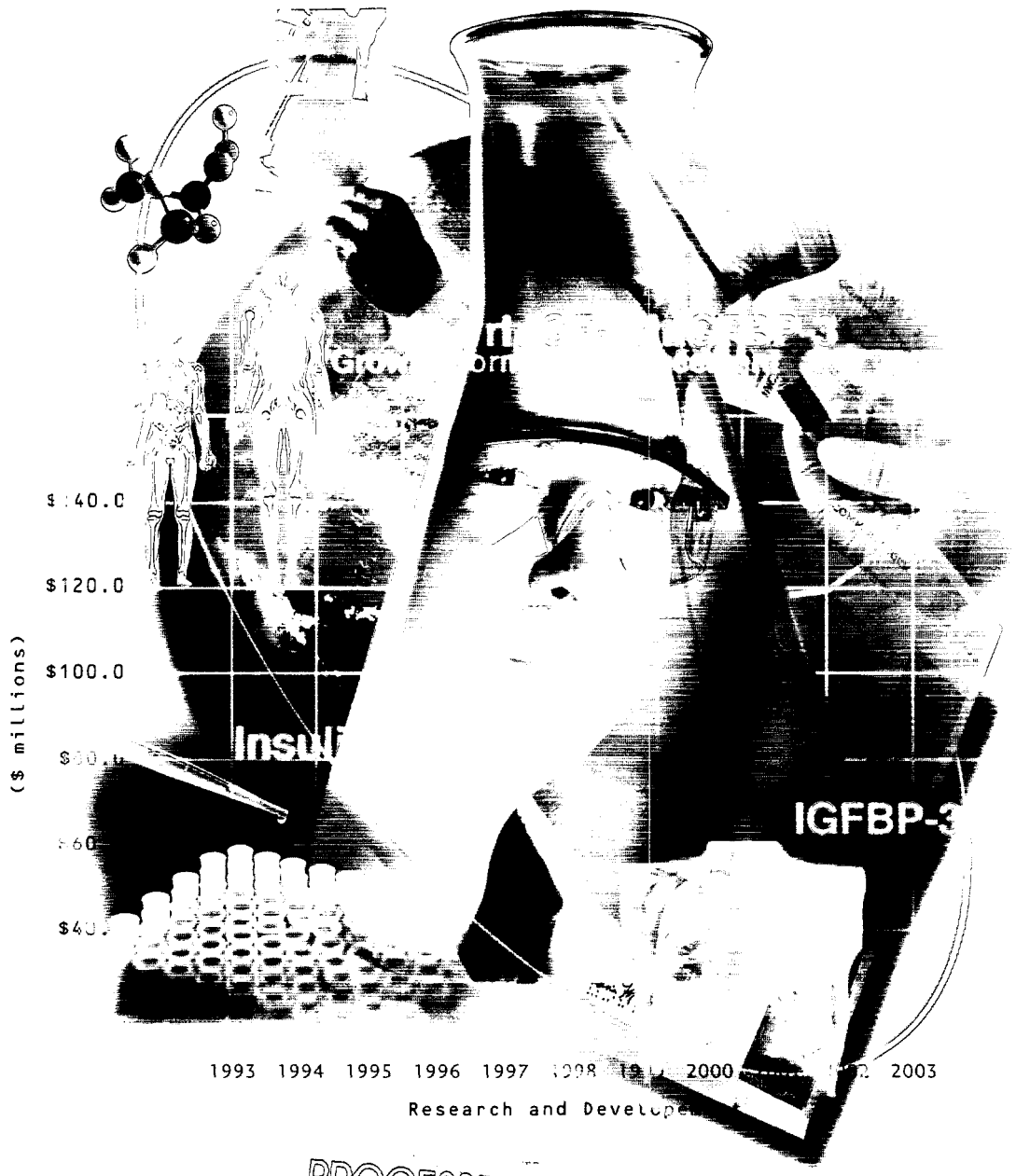
INSMED
INCORPORATED

2003 Annual Report



Developing
Medicines
to **Treat**
metabolic **diseases**
and endocrine
Disorders

Geoffrey Allan, Ph.D.
Chairman and Chief Executive Officer

developing
Treatments for
severe GROWTH disorders,
extreme INSULIN resistance,
and diabetes

Insmed is a biopharmaceutical company engaged in the development and commercialization of medicine for the treatment of metabolic diseases and endocrine disorders with unmet medical needs.

A MESSAGE FROM THE CHAIRMAN

2003 was a successful year for Insmed. The cornerstone of our achievements in 2003 was our discipline to adhere to a clearly defined corporate strategic plan. This plan included setting specific scientific and development objectives with our drug candidates SomatoKine® and rhIGFBP-3 while maintaining fiscal responsibility.

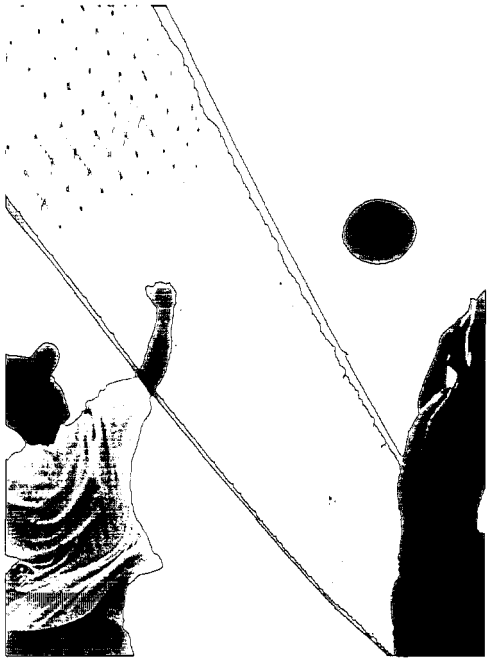
For SomatoKine®, we were able to successfully meet the regulatory requirements in several countries which allowed us to initiate our Phase III pivotal trial in Growth Hormone Insensitivity Syndrome (GHIS). In addition, we met with the U.S. Food and Drug Administration on several occasions to discuss our clinical plans and development strategy for SomatoKine®. We obtained Orphan Drug Designation with the European authorities for the use of SomatoKine® in the treatment of GHIS which complements our Orphan Drug Designation here in the U.S. We were also successful in establishing our named-patient program in GHIS and we now provide drug product to children suffering from this severe handicap. Although this program is of a limited nature, we are obtaining reimbursement for the drug product provided in this program, which, we believe, clearly establishes the need and value of this therapy. More importantly to Insmed is that this named patient program is laying the groundwork for commercialization of SomatoKine® by familiarizing physicians who treat this condition with the drug.

We also made significant advances with our second product candidate, rhIGFBP-3. We are developing rhIGFBP-3 as a novel treatment for various cancers. Experimental studies have demonstrated that rhIGFBP-3 enhances "standard of care" therapy and has shown comparable efficacy to other established treatments. rhIGFBP-3 mimics the naturally occurring IGFBP-3 and may not elicit the undesirable side effects that are characteristic of many cancer therapies on the market today.

We approach the future with confidence. Our executive management team has significant experience in drug development, enabling us to effectively manage the drug approval process. We currently possess the rights, through ownership and/or license, to worldwide patents covering methods of use and formulations of our product candidates. We will continue to develop our product candidates in human clinical trials with the goal of bringing safe, well-tolerated products to market.

As shareholders of Insmed, you share in our aspirations to create sustained value in our Company and bring much needed therapy to patients. I am honored to be engaged in such an important quest. I thank you for your support and look forward to updating you on our progress throughout the year.

Geoffrey Allan, Ph.D.
Chairman and Chief Executive Officer



GHIS is a severe GENETIC disorder in which patients,

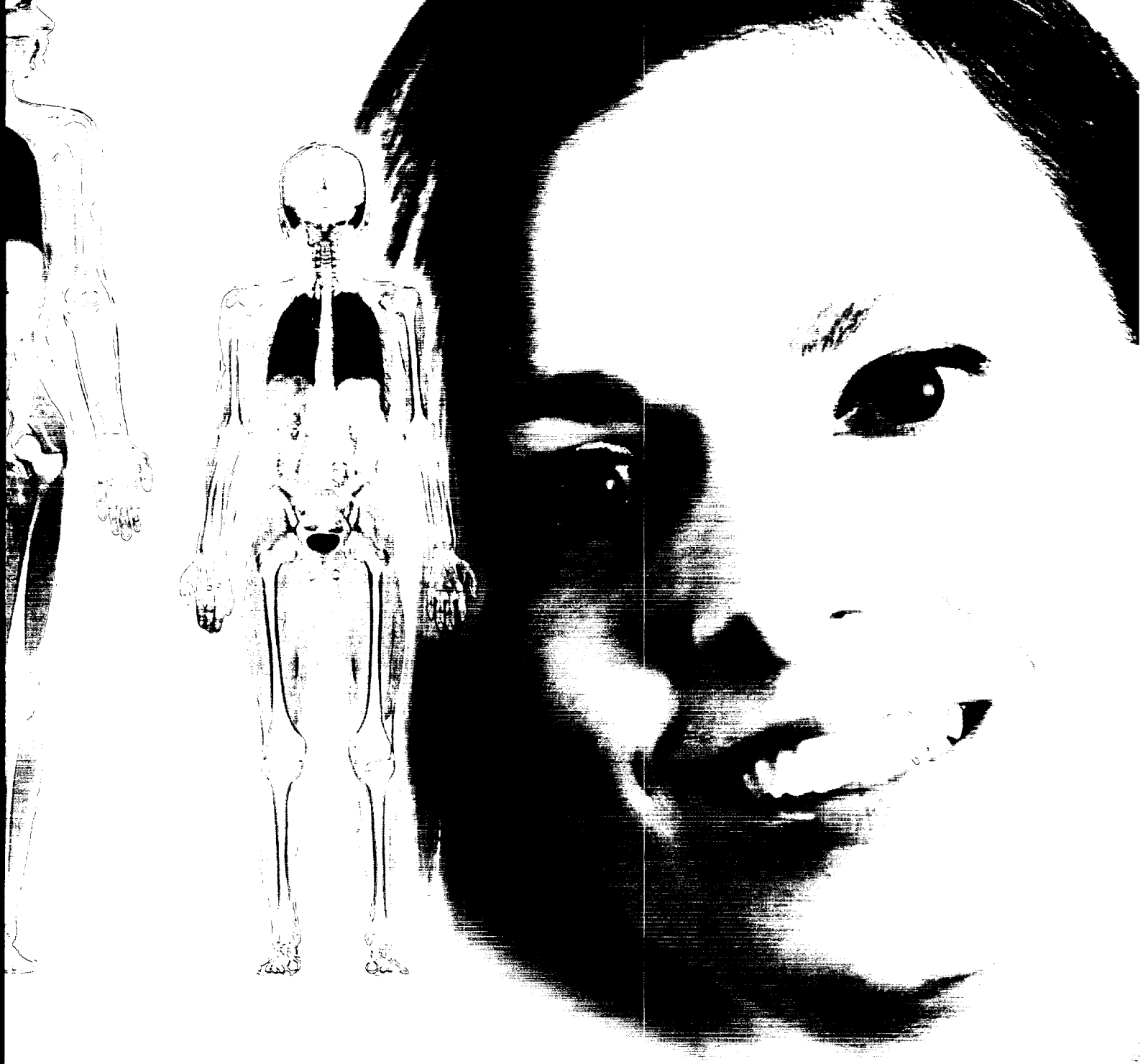
when exposed to growth hormone (GH), do not generate insulin-like growth factor-I (IGF-I), the mediator of many of the effects ascribed to GH. IGF-I is essential for proper growth and metabolism.

Ronald Gunn, M.S., M.B.A.
Executive Vice President and
Chief Operating Officer

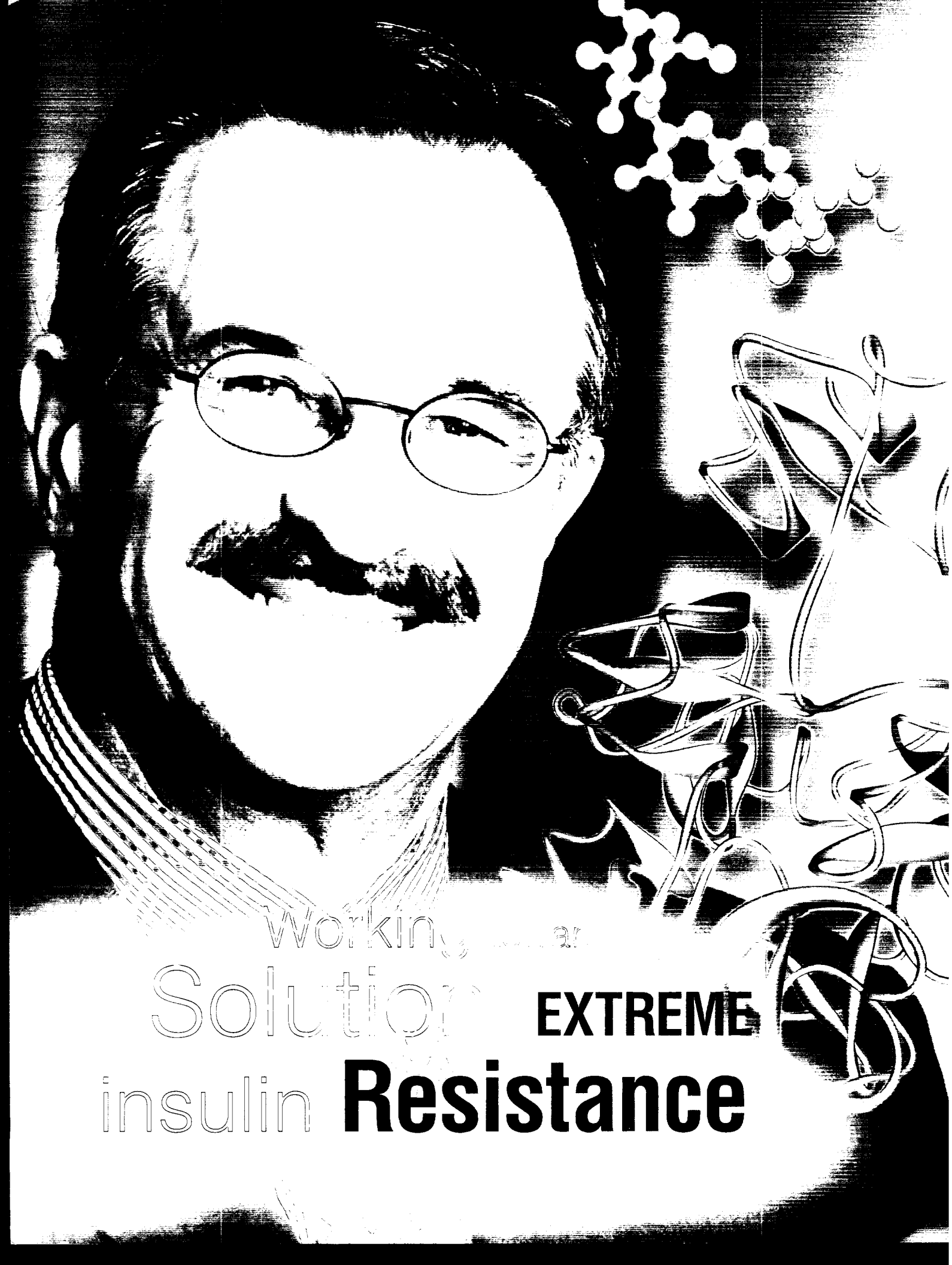
Insmed's drug candidate, SomatoKine® is a recombinant protein complex of insulin-like growth factor-I (IGF-I) and its most abundant binding protein, insulin like growth factor binding protein-3 (IGFBP-3). SomatoKine® is a novel, proprietary delivery composition of IGF-I. As a once-daily injection, SomatoKine® is designed to safely restore IGF-I levels in a physiologically relevant fashion. We believe we are positioned to build a near term commercial opportunity in the well defined niche GHIS market. Insmed is conducting a Phase III clinical trial with SomatoKine® to determine if administration of the drug will increase height velocity in subjects with GHIS.

"Insmed's SomatoKine® is potentially the safest IGF-I replacement therapy being developed, and may prove to be useful for the significant group of children who suffer from IGF-I deficient growth disorders."

Martin Savage, M.D.
Professor of Pediatric Endocrinology
St. Bartholomew's Hospital, London



Offering treatments for CHILDREN and Adolescents with GHIS


Working
Solution
EXTREME
insulin Resistance

PATIENTS with diabetes, over time, become less SENSITIVE to INSULIN

and require higher and higher amounts to maintain adequate control of blood glucose.

Anne Smith, Ph.D.
Manager, Biostatistics
and Data Management

IGF-I deficiency is a hallmark of the diabetes condition, and currently no approved IGF-I therapy is available for these patients who are failing insulin therapy in the United States. Insmed has conducted several Phase II studies in patients with diabetes, which demonstrated that as a once daily injection SomatoKine® can significantly improve insulin sensitivity and glucose control.

"SomatoKine® may prove to be very useful for the management of diabetic patients who cannot achieve adequate blood sugar control using insulin injections."

David Clemmons, M.D.
Chief of Endocrinology
University of North Carolina
School of Medicine

Over the next decade, ADVANCES in the treatment of Cancer

will come not only from improvements in traditional classes of therapies but also from the introduction of innovative therapies that display improved efficacy and toxicity profiles through a targeted approach.

Mark Sleevi, Ph.D.
Principal Scientist

As a naturally occurring anti-tumor agent, IGFBP-3 blocks the survival pathways associated with IGF-I and exerts IGF independent effects to induce the death of cancer cells. Insmed's patented, recombinant human insulin-like growth factor binding protein-3 (rhIGFBP-3) has demonstrated efficacy in numerous cancer indications, including breast, lung, colon and prostate cancers. Recent independent studies have demonstrated that rhIGFBP-3 can increase the efficacy of standard cancer therapies. Experimental studies performed by Insmed corroborate previously published reports regarding rhIGFBP-3's efficacy when administered alone or in combination with other anti-tumor agents.

"The ultimate goal for any cancer therapy is to force only cancer cells to commit suicide, but not the healthy cells of the patient. Very few current therapies have this advantage and our data suggests that rhIGFBP-3 has promise in conferring such selectivity."

Jeffrey Holly, Ph.D.
Director of Research
Bristol Royal Infirmary, U.K.

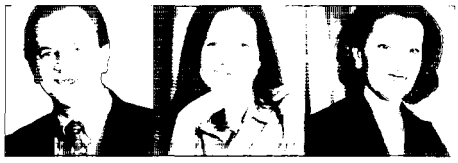
"rhIGFBP-3 has demonstrated significant anti-tumor activity alone and in combination with other agents in a variety of experimental settings providing proof-of-principle for the therapeutic use of this agent as a treatment for several cancers, in particular, prostatic carcinoma."

Pinchas Cohen, M.D.
Chief of Pediatric Endocrinology
David Geffen School of Medicine, UCLA

Developing

innovative TREATMENTS

for **CANCER**



Insmed Incorporated is a biopharmaceutical company engaged in the development and commercialization of medicines for the treatment of metabolic diseases and endocrine disorders with unmet medical needs. Our Approach is to Correct metabolic defects in the HUMAN BODY by replacing key regulatory MOLECULES in a physiologically relevant fashion. We believe this approach will translate into an intrinsic SAFETY advantage for our products.

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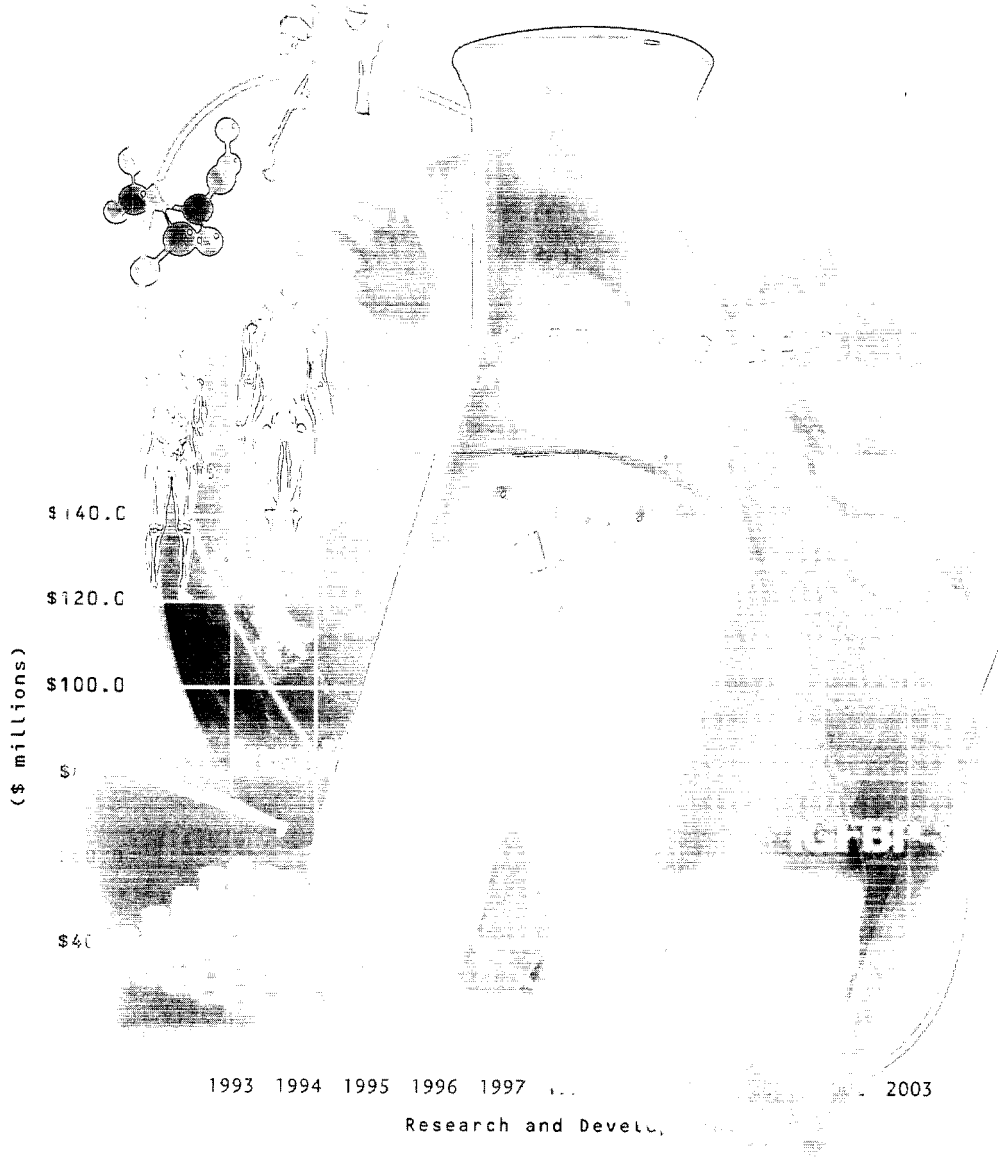
2003 Form 10-K



Developing
Medicines
to Treat
metabolic diseases
and endocrine
Disorders

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, 2003

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 (Address of principal executive offices) (zip code)	(804) 565-3000 (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

Preferred Stock Purchase Rights

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant on June 30, 2003 was $89,308,519 (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 29, 2004, there were 38,394,994 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, 2003, and to be delivered to shareholders in connection with the 2003 Annual Meeting of Shareholders, are incorporated in Part III by reference.

INSMED INCORPORATED

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REPORT: FORM 10-K

In this Form 10-K, the "Company," "Insmed," "Insmed Incorporated," "we," "us" and "our" refer to Insmed Incorporated, a Virginia corporation. 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

Overview

Insmed Incorporated is a biopharmaceutical company focused on the development and commercialization of drug products for the treatment of metabolic diseases and endocrine disorders. Our approach is to correct metabolic defects in the human body by replacing key regulatory molecules in a physiologically relevant fashion. We believe this will translate into an intrinsic safety advantage for our products in the marketplace. We currently have two lead drug candidates, recombinant human insulin-like growth factor-I bound to recombinant human insulin-like growth factor binding protein-3 (rhIGF-I/rhIGFBP-3; also known as SomatoKine) and rhIGFBP-3. We are actively developing these drugs to treat indications in the metabolic and oncology fields.

The endocrine system regulates metabolism through the use of hormones. IGF-I is a naturally occurring hormone necessary for normal growth and metabolism. Growth hormone (GH) regulates the cellular production of IGF-I, which mediates the majority of its growth-promoting effects. In the human body, IGF-I circulates in the bloodstream bound to a second protein called IGFBP-3, which serves to regulate the tissue distribution of IGF-I, therefore playing a major role in controlling its actions. GH deficiency (GHD) results in inadequate IGF-I production, which can result in growth disturbance in children. GH replacement therapy causes an increase in IGF-I levels and is used to successfully treat this condition. However, we believe many individuals have normal GH secretion, but because their cells are insensitive to this hormone they become IGF-I deficient and suffer from growth disturbance. Individuals with this condition are candidates for IGF-I replacement therapy. We believe that to ensure that IGF-I replacement is carried out in a physiologically relevant way, it is desirable to administer it bound to IGFBP-3, therefore maintaining the normal equilibrium of these important proteins in the bloodstream. rhIGF-I/rhIGFBP-3 is a recombinant protein complex that mimics the effects of IGF-I/IGFBP-3 in the bloodstream.

rhIGF-I/rhIGFBP-3 is currently in development for a number of metabolic and endocrine indications. The most advanced indication in development is the treatment of severe growth disturbance due to growth hormone insensitivity syndrome (GHIS) (i.e., Laron's Syndrome). In children, this condition is characterized by a height standard deviation score three standard deviations below normal and an IGF-I standard deviation score three standard deviations below normal. GHIS can lead to a range of other metabolic disorders, including lipid abnormalities, decreased bone density, obesity and insulin resistance.

We have been granted Orphan Designation by the United States Food and Drug Administration (FDA) and European Agency for the Evaluation of Medicinal Products (EMEA) for rhIGF-I/rhIGFBP-3 in the treatment of GHIS. A worldwide Phase III clinical trial for this indication is in progress.

We have been granted an exclusive license from Pharmacia (now Pfizer) to a large data base of historical treatment information and regulatory submissions associated with rhIGF-I. Pharmacia received approval of rhIGF-I for the treatment of GHIS in the majority of countries now in the European Union. We believe this exclusive license to Pharmacia's regulatory dossiers and other information will be of value to us during our product registration process for rhIGF-I/rhIGFBP-3. The data received through this license include results from 119 patients with GHIS who were treated intermittently for up to 14 years with rhIGF-I.

We believe the commercial opportunities for rhIGFI/rhIGFBP-3 reach beyond the indication of GHIS and that initial approval of our rhIGF-I/rhIGFBP-3 may offer us an opportunity to enter other potentially very large markets. These markets include other growth disturbances related to IGF-I deficiency, diabetes, myotonic dystrophy, HIV associated adipose redistribution syndrome, severe burns and hip fracture. It is our intention to initiate clinical studies in a variety of these indications with rhIGF-I/rhIGFBP-3. Based on the results from these studies we will select the next indication to pursue for marketing authorization.

Our oncology program focuses on IGFBP-3 as a naturally occurring anti-tumor agent. This protein is normally found in the human bloodstream and several epidemiological studies have demonstrated that cancer risk increases with decreasing blood levels of IGFBP-3. rhIGFBP-3 is a recombinant protein that mimics the effects of IGFBP-3 in the bloodstream. This product is currently in pre-clinical development for a variety of cancers including those of the breast, lung, colon and prostate.

Scientific Background

Role of IGF-I and IGFBP-3 in Growth

IGF-I is required for normal growth, development and metabolism. The role of IGFBP-3 is to control the activity and distribution of IGF-I. These proteins circulate as a complex and are normally produced as a result of a hormonal cascade beginning with the secretion of GH by the pituitary gland. GH binds to its receptor which initiates an intracellular signaling process resulting in the production of IGF-I and IGFBP-3. IGF-I is delivered to tissues to stimulate the growth of cartilage and bone.

Insufficient blood levels of either IGF-I or GH in childhood result in growth disturbance. Since the 1950s, children with low levels of GH and resulting growth disturbance have been treated with GH replacement therapy, resulting in IGF-I production and subsequent growth. However, there are children with growth disturbance who, despite normal levels of GH, have low levels of IGF-I. These children are IGF-I deficient usually because of abnormalities in either their GH receptors or in their GH signaling pathways. GHIS is one example of a condition that results from this abnormality.

Role of IGF-I and IGFBP-3 in Glucose Metabolism

Insulin is the primary hormone responsible for controlling glucose metabolism. The proper balance of insulin, GH and IGF-I is extremely important for normal glucose metabolism. Insulin and GH regulate production of IGF-I and IGFBP-3 by the liver. IGF-I elicits many of the physiological effects of insulin.

Several of our own short-term clinical studies with rhIGF-I/rhIGFBP-3 and several longer-term studies with rhIGF-I reported in scientific literature demonstrate that replacement of IGF-I reduces insulin requirements, improves glycemic control and improves insulin sensitivity in both type 1 and type 2 diabetes patients. Fujisawa Pharmaceutical Co., Ltd., with whom we have entered into a license agreement (see Strategic Relationships), has received approval of rhIGF-I in Japan for the treatment of the most severe forms of diabetes, often called extreme insulin resistance. Extreme insulin resistance describes a set of chronic diseases caused by inherited and/or acquired ineffectiveness of insulin.

Role of IGF-I and IGFBP-3 in Cancer

IGF-I plays an essential role in normal growth throughout fetal and childhood development. In adult life, IGF-I continues to function by regulating cellular metabolism, inducing cell division and protecting against cell death. IGFBP-3 is the most abundant naturally occurring IGF-I binding protein in the circulation and controls the actions of IGF-I by regulating its tissue distribution.

A number of epidemiological studies suggest that reduced circulating levels of IGFBP-3 or an increased ratio of IGF-I to IGFBP-3 are associated with an increased risk for the development of several common cancers, including those of the breast, prostate, lung and colon. Therefore, modulation of the IGF axis via administration of rhIGFBP-3 may represent a novel therapeutic approach to a variety of human cancers.

Insmed is currently engaged in an active pre-clinical program with prominent clinical oncologists and world experts in the field of IGFBP-3 research to develop rhIGFBP-3 as a therapeutic agent. To date, we have evaluated the efficacy of rhIGFBP-3 alone and in combination with standard chemotherapeutic agents in pre-clinical models of breast, lung and colon cancers. Our ongoing pre-clinical work is directed toward defining the optimal clinical protocol in which to translate these promising observations.

Product Pipeline

rhIGF-I/rhIGFBP-3 (SomatoKine®):

Therapeutic Category	Therapeutic Indication	Phase of Development
Growth / Developmental Disorders	GHIS	Phase III
	Other Growth Disorders Associated with IGF-I Deficiency	Phase II planned
	Retinopathy of Prematurity	Phase I planned
Insulin Resistance / Diabetes	Extreme insulin resistance	Phase II planned
	Type 1 Diabetes	Phase II
	Type 2 Diabetes	Phase II
Other Metabolic / Neurological	HIV Associated Adipose Redistribution Syndrome (HARS)	Phase II planned
	Myotonic Dystrophy	Phase II planned
Recovery from Trauma / Surgery	Recovery from Severe Burn Trauma	Phase II
	Recovery from Osteoporotic Hip Fracture Surgery	Phase II

rhIGFBP-3:

Therapeutic Category	Therapeutic Indication	Phase of Development
Oncology	Breast Cancer	Phase I planned
	Other cancer types: colorectal, prostate and lung	Pre-clinical

Primary Therapeutic Indications

Growth Disturbance Due to IGF-I Deficiency

GHIS is a condition affecting a specific subset of patients suffering from growth disturbance because of a deficiency in IGF-I. This deficiency is due to a defect in the GH receptor or signaling pathway. Characteristics of this condition include:

- normal or elevated serum GH levels;
- inability to generate normal IGF-I levels after GH provocation;
- reduced IGF-I and IGFBP-3 serum levels;
- severe postnatal growth failure and markedly reduced adult height (120-130cm; 4ft);
- truncal adiposity;
- delayed skeletal maturation;
- abnormal craniofacial development;
- microphallus in boys; and
- slightly delayed puberty.

Physicians use a height standard deviation score, or height SDS, to indicate how many standard deviations a person's height is from the average of the normal population of a similar age and gender. The American Academy of Pediatrics and the American Academy of Clinical Endocrinology define short stature as a height that is more than two standard deviations below the average. Similarly, in evaluating IGF-I deficiency, physicians can

use an IGF-I SDS to indicate how many standard deviations a person's IGF-I level is below the average level of the population of a similar age and gender.

Extreme Insulin Resistance

Insulin resistance can be described as an abnormality caused by the ineffectiveness of insulin to complete its metabolic function. This abnormality can occur in many forms and results in varying degrees of disease severity. Several types of extreme insulin resistance result from genetic defects in the insulin receptor gene and/or in other genes involved in insulin signal transduction. These conditions include:

- Type A and Type B Syndrome,
- Rabson-Mendenhall Syndrome, and
- Leprechaunism.

Type A Syndrome patients have high circulating concentrations of insulin with impaired glucose tolerance or diabetes. They are also hyperandrogenic and experience many of the side effects associated with this condition such as hirsutism, acne, abnormal menstruation and infertility. High doses of insulin fail to provide adequate glycemic control in these patients and there is no satisfactory treatment currently available. Death in adulthood most often is due to cardiovascular and renal complications.

Type B Syndrome is characterized by the presence of autoantibodies to the insulin receptor which interfere with proper receptor functioning. These patients also have high circulating concentrations of insulin with alternating episodes of hyperglycemia and hypoglycemia. They are hyperandrogenic and commonly experience hirsutism, polycystic ovaries, acanthosis nigricans and lipoatrophy. These patients often have additional autoimmune disorders such as systemic lupus erythermatosus. High doses of insulin fail to provide adequate glycemic control in these patients and there is no satisfactory treatment currently available. Death past middle age most often occurs due to hypoglycemia and lupus.

Rabson-Mendenhall Syndrome patients also have high circulating concentrations of insulin with alternating episodes of hyperglycemia and hypoglycemia. They are also hyperandrogenic and commonly experience hirsutism, polycystic ovaries, acanthosis nigricans and growth disturbance. High doses of insulin fail to provide adequate glycemic control in these patients and there is no satisfactory treatment currently available. Death at 1-15 years of age most often occurs due to ketoacidosis.

Leprechaunism patients also have high circulating concentrations of insulin with alternating episodes of hyperglycemia and hypoglycemia. They are also hyperandrogenic and commonly experience hirsutism and polycystic ovaries. They are characterized by severe intrauterine and postnatal growth retardation. High doses of insulin fail to provide adequate glycemic control in these patients and there is no currently satisfactory treatment available. Death at less than one year of age most often occurs due to vascular, respiratory and other complications.

Diabetes

Patients with type 1 diabetes are characterized by their inability to produce insulin. In these patients, insulin deficiency leads to abnormalities in the GH/IGF-I/insulin axis. This deficiency may result in down-regulation of GH receptors in the liver, resulting in reduced circulating IGF-I levels. Low circulating IGF-I levels inhibit the negative feedback loop to the pituitary causing GH hypersecretion. This condition is associated with decreased insulin sensitivity and worsening of metabolic control. Since the liver is the primary site of insulin stimulated IGF-I production, peripheral administration of insulin cannot completely correct this phenomenon.

Patients with type 2 diabetes are characterized by the inability of the insulin they produce to work effectively. In addition to low circulating levels of IGF-I, these patients have an increased number of insulin/IGF-I hybrid receptors. Increased expression of these hybrid receptors positively correlates with a decrease in both insulin binding affinity and insulin sensitivity.

Diabetes related complications include retinopathy, heart disease, kidney failure and neuropathy. Diabetic retinopathy is the leading cause of blindness. Heart disease accounts for approximately 50% of all deaths among diabetics in industrialized countries. Diabetes is among the leading causes of kidney failure. Fifty percent of people with diabetes have some degree of neuropathy, which can lead to sensory loss, impotence, limb damage and amputation.

Cancer

The World Health Organization estimates that by 2020, the number of annual worldwide cancer related deaths is expected to reach 10 million. To date the FDA has approved over 110 oncology drugs for more than 25 indications. Up to two-thirds of these drugs are cytotoxic agents, many of which exhibit significant systemic toxicity and decrease the quality of life of the patient.

Identification of the signaling pathways that regulate tumor growth has led to novel strategies for the treatment of cancer. As a result, new agents that target growth factors and their receptors are emerging as promising new treatments.

Business Strategy

Our goal is to focus on product development and commercialization of products for the treatment of metabolic and endocrine diseases. Our initial focus is on obtaining the approval of rhIGF-I/rhIGFBP-3 for the treatment of GHIS and establishing proof-of-concept clinical data with rhIGFBP-3 in the treatment of breast cancer. Our long-term strategy is to capitalize on many other potential endocrine and metabolic indications with rhIGF-I/rhIGFBP-3 and additional cancer indications with rhIGFBP-3. Key elements of our strategy for achieving these goals include:

Seek FDA and EMEA approval of rhIGF-I/rhIGFBP-3 replacement treatment for GHIS. We are currently conducting a Phase III clinical trial in patients with GHIS and plan to submit a New Drug Application (NDA) to the FDA and a Marketing Authorization Application (MAA) to the EMEA for this indication. Children with this disorder have a significant unmet medical need because no effective treatment is currently available on the market. The proprietary information we have licensed from Pharmacia demonstrates that replacement therapy with rhIGF-I given twice daily will significantly improve height velocity in these severely growth disturbed patients. Data from our clinical studies demonstrates that we can achieve equivalent circulating concentrations of IGF-I following administration of rhIGF-I/rhIGFBP-3 as was achieved in the Pharmacia studies following administration of rhIGF-I. Furthermore, these blood levels were achieved with one injection of rhIGF-I/ rhIGFBP-3 per day as opposed to the two injections needed with rhIGF-I alone. In addition to having the advantage of once-a-day dosing, our animal data suggest fewer side effects with rhIGF-I/rhIGFBP-3 when compared with rhIGF-I.

We currently have an agreement with Avecia Limited, a third party contract manufacturer in the United Kingdom, to produce our rhIGF-I/rhIGFBP-3 drug substance. Based on discussions with the FDA, we are planning to conduct several studies, including analytical, pre-clinical and clinical, to compare the drug substance previously used in our pre-clinical and clinical programs to the new drug substance produced by Avecia. The results of this comparison will become part of our submission to the regulatory authorities.

Expand the GHIS indication to other growth disorders related to IGF-I deficiency. A number of growth disorders related to IGF-I deficiency other than GHIS represent conditions with significant unmet medical needs. While seeking approval in GHIS, we plan to investigate these other indications and further develop those that will provide the best market opportunity for label expansion. We will then seek this label expansion through supplemental regulatory submissions. It is likely that we will conduct one or more pre-clinical and clinical studies to support label expansion.

Develop rhIGF-I/rhIGFBP-3 in additional indications. We intend to initiate clinical studies of rhIGF-I/rhIGFBP-3 in additional indications. Based on the data from these studies, we will select the most promising indications for further development and commercialization. The indications we are considering are extreme insulin resistance, diabetes, myotonic dystrophy, HIV associated adipose redistribution syndrome, recovery from severe burn injury, recovery from osteoporotic hip fracture and retinopathy of prematurity.

Establish a sales and marketing organization for the United States. We intend to develop a sales and marketing force to target the approximately 400 active U.S.-based pediatric endocrinologists who treat children with growth disorders. These physicians are primarily hospital-based and concentrated in major metropolitan areas and we believe that they will be best served by a focused marketing organization and specialized sales force. In addition, we intend to conduct continuing medical education programs, medical symposia, and regional speaker programs aimed at establishing awareness of rhIGF-I/rhIGFBP-3 in the medical community. We also intend to conduct post-marketing studies and establish a patient registry to provide further data on the safety and efficacy of rhIGF-I/rhIGFBP-3.

Establish a sales and marketing organization or obtain a Marketing Partner for Europe. We are exploring several opportunities in Europe to establish our own sales and marketing organization, acquire a sales and marketing organization and partner with an established sales and marketing organization. Our selected method for commercializing rhIGF-I/rhIGFBP-3 will be based on an analysis to determine which avenue provides the best long-term return for our investors. We expect to conduct continuing medical education programs, medical symposia, and regional speaker programs aimed at establishing awareness of rhIGF-I/rhIGFBP-3 in the European physician community. We also intend to conduct post-marketing studies and establish a patient registry to provide further data on the safety and efficacy of rhIGF-I/rhIGFBP-3.

Initiate clinical studies with rhIGFBP-3. Based on pre-clinical data we believe there is sufficient scientific evidence to proceed with clinical studies of rhIGFBP-3. Our strategy is to establish the pharmacokinetic profile of rhIGFBP-3 in a Phase I clinical study and then proceed to Phase II clinical studies in one or more of the following cancer types: breast, colorectal, lung and/or prostate.

Broaden endocrinology and oncology portfolio based on our expertise. Our longer-term strategy for growth is to pursue the development and commercialization of additional products for the treatment of significant unmet medical needs that complement our activities within the fields of metabolic and endocrine diseases and oncology.

Retain commercial rights to market products in selected markets. Our goal is to retain relevant marketing rights to our products and commercialize them in selected niche markets.

Establish corporate partnerships in certain markets. We plan to establish corporate partnerships to develop, market and commercialize our products in markets outside of our core focus.

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. Our focus is principally in developing and commercializing late-stage products. We conduct very little of our own pre-clinical laboratory research. However, we actively maintain ongoing discussions with academic research institutions and other companies regarding rhIGF-I/rhIGFBP-3, rhIGFBP-3 and other projects in endocrinology and oncology. We are currently conducting a Phase III clinical study with our lead product, rhIGF-I/rhIGFBP-3, and plan to investigate other potential indications with this product. We are also conducting pre-clinical studies with our other lead compound, rhIGFBP-3, and plan on conducting clinical studies with this product in the future. Our research and development expenses were approximately $7.1 million in 2003, $18.1 million in 2002, and $35.5 million in 2001.

Strategic Relationships

Avecia Limited

In May 2002, we entered into an agreement with Avecia Limited, Europe's largest privately held specialty chemical company, for the process development and manufacture of rhIGF-I/rhIGFBP-3. In consideration for this process development and manufacturing agreement, we are obligated to pay success fees for milestones and process development and manufacturing costs associated with the ongoing production of rhIGF-I/rhIGFBP-3.

Pharmacia Inc.

Pharmacia, Inc. was granted marketing approval in several European and Scandinavian countries for rhIGF-I in the treatment of GHIS. In October 2002, we entered into an agreement with Pharmacia that grants us an exclusive worldwide license to Pharmacia's portfolio of regulatory filings and proprietary information pertaining to rhIGF-I for the treatment of GHIS. We have made a commitment to make rhIGF-I/rhIGFBP-3 available on a named patient basis to GHIS subjects that were previously being treated with rhIGF-I supplied by Pharmacia.

Fujisawa Pharmaceutical Co., Ltd.

In January 2004, Insmed was granted a non-exclusive license to patent rights pertaining to the use of IGF-I therapy for the treatment of extreme or severe insulin resistant diabetes from Fujisawa Pharmaceutical Co., Ltd. Under the terms of the agreement, Insmed will obtain worldwide rights in territories (excluding Japan) where a valid patent claim exists, including the United States and Europe. We have made a commitment to use reasonable commercial efforts to make rhIGF-I/rhIGFBP-3 available on a named patient basis to patients with extreme insulin resistance.

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 issue in the United States or in foreign countries. There also can be no assurance that United States or foreign patents issuing from any of these applications will not later be held invalid or unenforceable.

We hold 28 United States issued or allowed patents related to the composition, production, antibodies and methods of use for rhIGF-I/rhIGFBP-3 and rhIGFBP-3, including:

- Two issued patents for rhIGFBP-3 composition-of-matter;
- 15 therapeutic use patents for rhIGF-I/rhIGFBP-3, IGF-I, rhIGFBP-3 or rhIGFBP-3 fragments for the treatment of various disease conditions; and
- 11 patents regarding novel expression, production or analysis methods, some of which may be used for the manufacture of rhIGF-I/rhIGFBP-3 and pharmaceutical compositions of rhIGF-I/rhIGFBP-3.

Many of the above patents have been issued or are pending issue in the major pharmaceutical markets including Canada, Japan and Europe.

As part of the ongoing development of rhIGF-I/rhIGFBP-3 and rhIGFBP-3, 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 rhIGF-I/rhIGFBP-3 and rhIGFBP-3 compositions, methods of production and methods of treatment expire at various times during the years 2010 through 2019.

As part of our development and manufacturing agreement with Avecia Limited, we have obtained certain non-exclusive rights to Avecia's proprietary manufacturing technology. In January 2004, Insmed was granted a non-exclusive license to patent rights pertaining to the use of IGF-I therapy for the treatment of extreme or severe insulin resistant diabetes from Fujisawa Pharmaceutical Co., Ltd.

There has been increasing litigation in the biopharmaceutical industry with respect to the manufacture and sale of new therapeutic products. The validity and breadth of claims in biotechnology patents may involve complex factual and legal issues for which no consistent policy exists. In particular, the patent protection available for protein-based products, such as rhIGF-I/rhIGFBP-3 and rhIGFBP-3, is highly uncertain and involves issues relating to the scope of protection of claims to gene sequences and the production of their corresponding proteins.

In 1998 Genentech requested a hearing with the European Patent Office to oppose the validity of one of our European patents with claims to rhIGFBP-3, uses of rhIGFBP-3 and uses of rhIGF-I/rhIGFBP-3. As of yet, no hearing date has been set by the European Patent Office. Should the opposition hearing be held and should Genentech prevail, some or all of the claims of this patent may be revoked. This result could lessen our ability to exclude others, but would not affect our own ability to practice these claims.

Third parties, including Genentech, Chiron, Amgen, Novartis AG, and Robert Rieveley hold United States and/or foreign patents possibly directed to the composition, production and/or use of rhIGF-I, rhIGFBP-3, rhIGF-I/rhIGFBP-3 and/or recombinant proteins in general. After examining these patents, we do not believe they present an obstacle to our plans to commercialize rhIGF-I/rhIGFBP-3 and rhIGFBP-3. However, we can provide no assurance that any one of these third parties will not assert in the future a contrary position, for instance in the context of an infringement action. Moreover, while we cannot predict with certainty the outcome of such a proceeding, an adverse ruling could impact our ability to make, use or sell our products.

In some cases, litigation or other proceedings may be necessary to defend against claims of infringement, to enforce patents licensed to us, to protect our know-how or other intellectual property rights or to determine the scope and validity of the proprietary rights of third parties. Any potential litigation could result in substantial cost to us and diversion of our resources. We cannot be sure that any of our licensed patents will ultimately be held valid. An adverse outcome in any litigation or proceeding could subject us to significant liability.

We generally enter into confidentiality agreements with our employees and consultants. Our confidentiality agreements generally require our employees and consultants to hold in confidence and not disclose any of our proprietary information. Despite our efforts to protect our proprietary information, unauthorized parties may attempt to obtain and use our proprietary information. Policing unauthorized use of our proprietary information is difficult, and the steps we have taken might not prevent misappropriation, particularly in foreign countries where the laws may not protect our proprietary rights as fully as do the laws of the United States (U.S.).

Manufacturing

We currently rely on contract manufacturers to produce rhIGF-I/rhIGFBP-3 and rhIGFBP-3. Our product candidates will need to be manufactured in a facility by processes that comply with current good manufacturing practices (cGMP) 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 and/or product commercialization may be adversely affected.

rhIGF-I/rhIGFBP-3 is a complex of two proteins, rhIGF-I and its binding protein rhIGFBP-3, 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. During the manufacturing process, rhIGF-I and rhIGFBP-3 are produced separately and then combined to make rhIGF-I/rhIGFBP-3. The rhIGFBP-3 can either be utilized to make rhIGF-I/rhIGFBP-3 or kept separate as its own distinct product.

To date, we have supplied all of our pre-clinical and clinical Phase II study requirements with rhIGF-I/rhIGFBP-3 previously produced by our subsidiary, Celtrix. Since Celtrix no longer produces rhIGF-I/rhIGFBP-3, we have identified a new source for this compound for clinical trial and commercial use. We have an agreement with Avecia Limited to manufacture rhIGF-I/rhIGFBP-3 at Avecia's site at Billingham, England. We cannot guarantee that Avecia will be able to produce the rhIGF-I/rhIGFBP-3 or rhIGFBP-3 necessary for future pre-clinical and clinical trials or commercialization.

Marketing and Sales

We currently have no sales, marketing or distribution capability. However, we intend to develop a sales and marketing force to target the approximately 400 active U.S.-based pediatric endocrinologists who treat children with growth disturbance. Because these pediatric endocrinologists are primarily hospital-based and concentrated in major metropolitan areas, we believe that a focused marketing organization and specialized sales force can effectively serve them. In addition, we intend to conduct continuing medical education programs, medical symposia, and regional speaker programs aimed at establishing awareness of rhIGF-I/rhIGFBP-3 in the physician community. We also intend to conduct post-marketing studies and establish a patient registry to provide further data on the safety and efficacy of rhIGF-I/rhIGFBP-3.

We are exploring several opportunities for sales and marketing in Europe including the establishment of our own sales and marketing organization, acquisition of an existing sales and marketing organization and partnering with an established sales and marketing organization.

Our goal is to retain marketing, sales and distribution rights to our product candidates for certain niche markets and find commercial partners to develop and market our products in markets outside of our core focus.

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.

Currently, no drug in the U.S. or Europe is approved and marketed as replacement therapy for the treatment of GHIS. Other than Insmed, we are aware of only one other company, Tercica, Inc., that is pursuing development of a product for this indication. Tercica, in documents filed with the Securities and Exchange Commission, has stated that it plans to submit a NDA for the use of rhIGF-I in the treatment of severe pediatric IGF deficiency in 2005. We believe this indication would include patients with GHIS. We believe Tercica may

also be planning to develop rhIGF-I for some of the same indications that we plan to pursue with rhIGF-I/rhIGFBP-3.

GH may also be a competitive product for the treatment of some patients with growth disorders associated with IGF-I deficiency. The major suppliers of commercially available GH are Genentech, Eli Lilly, Novo Nordisk, Pfizer and Serono.

In addition, we believe that Genentech, Merck, Novo Nordisk and Pfizer have previously conducted research and development of orally available small molecules that cause the release of GH, known as GH secretagogues. We are not aware of any continued clinical development of these molecules by these companies. We believe that Rejuvenon Corporation may have licensed certain rights to Novo Nordisk's GH secretagogues, which are in pre-clinical development. We are also aware that Theratechnologies is developing various peptides that stimulate the release of hormones that could be used in the treatment of some of the indications we plan to pursue with rhIGF-I/rhIGFBP-3.

Many companies are seeking to develop products and therapies for the treatment of diabetes. Our competitors include multinational pharmaceutical companies, specialized biotechnology firms, and universities and other research institutions. Our largest competitors include Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, Merck, Novartis, Novo Nordisk, Takeda Chemical Industries and Amylin Pharmaceuticals. Various products are currently available to treat type 2 diabetes, such as insulin and oral hypoglycemic drugs.

In addition, several companies are developing various new approaches to improve the treatments of type 1 and type 2 diabetes. Amylin Pharmaceuticals has conducted and is continuing to conduct clinical trials for two products, Symlin and Exenatide, for the treatment of type 2 diabetes. Tercica has indicated that it plans to pursue the development of rhIGF-I in the treatment of severe forms of diabetes.

Many companies are pursuing the development of products for the treatment of cancer. Our competitors include multinational pharmaceutical companies, specialized biotechnology firms, and universities and other research institutions. Although we are unaware of any companies developing rhIGFBP-3 for cancer, we are aware of companies who are developing products that are intended to target the same pathway that we are targeting with rhIGFBP-3.

It is possible that there are other companies with products currently in development or that exist on the market that may compete directly with rhIGF-I/rhIGFBP-3 or rhIGFBP-3.

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 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 of an Investigational New Drug Application (IND);
- Adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication;
- The submission of a NDA; and
- Regulatory 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 IND. The FDA

requires a 30-day waiting period after the filing of each IND 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 IND 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 pharmacokinetics and safety.

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. 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.

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 may 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.

The FDA's policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our products. We cannot predict the likelihood, nature or extent of adverse governmental regulation which might arise from future legislative or administrative action, either in the U.S. or abroad.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Orphan drug designation must be requested before submitting a NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and

approval process. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease, except in very limited circumstances, for seven years. This exclusivity, however, also could block the approval of our products for seven years if a competitor is granted orphan designation and receives NDA approval of the same drug for the same indication or disease before we do. We have received orphan designation for the treatment of severe burn injury, growth disturbances due to GHIS, and extreme insulin resistance. We also intend to file for orphan drug designation for other indications which meet the criteria for orphan exclusivity. Obtaining FDA approval to market a product with orphan drug exclusivity may not provide us with a material commercial advantage.

The FDA Modernization Act of 1997 included a pediatric exclusivity provision that was extended by the Best Pharmaceuticals for Children Act of 2002. Pediatric exclusivity is designed to provide an incentive to manufacturers for conducting research about the safety of their products in children. Pediatric exclusivity, if granted, provides an additional six months of market exclusivity in the United States for new or currently marketed drugs, if certain pediatric studies requested by FDA are completed by the applicant. We believe our current plans to study rhIGF-I/rhIGFBP-3 in children may qualify rhIGF-I/rhIGFBP-3 for the additional six months of pediatric exclusivity, although there can be no assurances that FDA will grant such additional exclusivity. The current pediatric exclusivity provision is scheduled to end on October 1, 2007 and there can be no assurances that it will be reauthorized.

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

Employees

As of December 31, 2003, we had 20 full-time employees. Of these employees, 12 were engaged in research and development and 8 were engaged in general management, finance and administration. None of our employees are 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 Item 7 under the section 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.

Since we have a limited operating history, a history of operating losses and an expectation that we will 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 currently have no commercial sales. We have incurred losses each year of operation and we expect 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 activities. 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, 2003, our accumulated deficit was $186.5 million. For the year ended December 31, 2003, our consolidated net loss was $10.3 million.

We currently have two lead product candidates, recombinant human (rh) IGF-I/rhIGFBP-3 (also known as SomatoKine) and rhIGFBP-3. rhIGF-I/rhIGFBP-3 is currently in development for a number of metabolic and endocrine indications. The most advanced indication in development is the treatment of severe growth disturbance due to growth hormone insensitivity syndrome (GHIS). Our second compound, rhIGFBP-3, is currently in pre-clinical development for a variety of cancers including breast, lung, colon and prostate.

All of our products are currently in the research and development stage and if we are unable to commercialize them it will adversely affect our business, financial condition and results of operations.

All of our potential products are in the research and development stage. Our long-term viability and growth depend on the successful commercialization of products which lead to revenue and profits. In order to commercialize any of our products they must first be successfully developed. Pharmaceutical product development is an expensive, high risk, lengthy, complicated, resource intensive process. In order to succeed, among other things, we must be able to:

- identify potential drug product candidates;
- design and conduct appropriate laboratory, pre-clinical and other research;
- submit for and receive regulatory approval to perform clinical studies;
- design and conduct appropriate clinical studies;
- select and recruit clinical investigators;
- select and recruit subjects for our studies;
- collect, analyze and correctly interpret the data from our studies;
- submit for and receive regulatory approvals for marketing; and
- manufacture the drug product candidates according to current good manufacturing practices (cGMP).

The development program with respect to any given product will take many years and thus delay our ability to generate profit. 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 require significant additional testing or turn out to be:

- unsafe;
- not effective;
- too difficult or expensive to manufacture;
- too difficult to administer; or
- unstable.

In order to conduct the development programs for our potential products we must, among other things, be able to successfully:

- raise sufficient money to pay for the development;

- attract and retain appropriate personnel; and
- develop relationships with other companies to perform various development activities that we are unable to perform.

Even if we are successful in developing our products, there are numerous developments that could prevent the successful commercialization of the products such as:

- the regulatory approvals of our products are delayed or we are required to conduct further research and development with our products prior to receiving regulatory approval;
- we are unable to build a sales and marketing group to successfully launch and sell our products;
- we are unable to raise the additional funds needed to successfully develop and commercialize our products or acquire additional products for growth;
- an event such as a lawsuit or other litigation drains our cash;
- we are unable to manufacture the quantity of product needed in accordance with current good manufacturing practices to meet market demand or at all;
- our product is determined to be ineffective or unsafe following approval and is removed from the market or we are required to perform additional research and development to further prove the safety and effectiveness of the product before re-entry into the market;
- competition from other products or technologies prevents or reduces market acceptance of our products;
- we do not have and cannot obtain the intellectual property rights needed to manufacture or market our products without infringing on another company's patents; or
- we are unable to obtain reimbursement for our products or such reimbursement may be less than is necessary to produce a reasonable profit.

Our growth strategy includes the commercialization of more than one product. We may not be able to identify and acquire complementary products, businesses or technologies and if acquired or licensed, they might not improve our business, financial condition or results of operations.

The failure to successfully acquire, develop and commercialize products will adversely affect our business, financial condition and results of operations.

If our products fail in pre-clinical or clinical trials or if we cannot enroll enough patients to complete our clinical trials, such failure may adversely affect our business, financial condition and results of operations.

In order to sell our products, we must receive regulatory approval. 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. 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. If our products fail in pre-clinical or clinical trials, it will have an adverse effect on our business, financial condition and results of operations.

We are currently conducting a Phase III clinical trial of rhIGF-1/rhIGFBP-3 in patients with GHIS and plan to include the data from this trial as a pivotal piece of information in a New Drug Application (NDA) submission to the United States Food and Drug Administration (FDA) and in a Marketing Authorization Application (MAA) to the European Agency for the Evaluation of Medicinal Products (EMEA). We must receive approval of these

applications before we can market rhIGF-I/rhIGFBP-3 in the respective territories. We are also planning clinical trials with rhIGFBP-3.

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

- investigator identification and recruitment;
- regulatory approvals to initiate study sites;
- 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 commercialization and sales, if any, of our products. Such delays could materially adversely affect our business, financial condition and results of operations.

We may be required to conduct broad, long-term clinical trials to address concerns that the long-term use of rhIGF-I/rhIGFBP-3 in broader chronic indications might increase the risk of diabetic retinopathy. This may adversely affect our business, financial condition and results of operations.

In previously published clinical trials of rhIGF-I, concerns were raised that long-term use of rhIGF-I might lead to an increased incidence and/or severity of retinopathy, a disease of new blood vessel growth in the eye which results in loss of vision. Because our product contains rhIGF-I, the FDA may require us to conduct broad, long-term clinical trials to address these concerns prior to receiving FDA approval for broad chronic indications such as diabetes. These clinical trials would be expensive and could delay our commercialization of rhIGF-I/ rhIGFBP-3 for these broader chronic indications. Adverse results in these trials could prevent our commercialization of rhIGF-I/rhIGFBP-3 for broad chronic indications or could jeopardize existing development and approvals in other indications.

We cannot be certain that we will obtain any regulatory approvals in the United States and Europe. The failure to obtain such approvals may materially adversely affect our business, financial condition and results of operations.

We are required to obtain various regulatory approvals prior to studying our drug products in humans and then again before we market and distribute our products. The regulatory review and approval process required to perform a clinical study in both the U.S. and Europe includes evaluation of pre-clinical studies and clinical trials, as well as the evaluation of our manufacturing process and is complex, lengthy, expensive, resource intensive and uncertain. Securing regulatory approval to market our products also requires the submission of extensive pre-clinical and clinical data, manufacturing information regarding the process and facility, scientific data characterizing our product and other supporting data to the regulatory authorities in order to establish its safety and effectiveness. This process is also complex, lengthy, expensive, resource intensive and uncertain. We have limited experience in filing and pursuing applications necessary to gain these regulatory approvals.

Data submitted to the regulators is 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 product. 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.

We are currently conducting a Phase III clinical trial of rhIGF-I/rhIGFBP-3 in patients with GHIS and plan to include the data from this trial as a pivotal piece of information in a NDA submission to the FDA and in a MAA submission to the EMEA. We must receive approval of these applications before we can market rhIGF-I/ rhIGFBP-3.

As part of our normal development we continue to increase our scale of production and refine our manufacturing process. Because of these changes we are required to perform various comparability analyses to demonstrate that the drug product used in our previous development studies is essentially the same as the new drug product produced. We have had several discussions with the FDA and other foreign regulatory agencies regarding our Phase III clinical study and this comparability analysis and believe we understand what is required to satisfy the FDA and EMEA. We plan to submit this data to the appropriate regulatory authorities as part of the regulatory process. If we are unable to produce comparable drug product or meet the regulatory requirements of comparability it will materially adversely affect our business, financial condition and results of operations.

The regulatory authorities have substantial discretion in the approval process and may either refuse to accept our applications, or may decide after review of our applications that our data is insufficient to allow approval of rhIGF-I/rhIGFBP-3. If the FDA or EMEA do not accept or approve our application, it may require that we conduct additional clinical, pre-clinical or manufacturing studies and submit that data before it will reconsider our application. This could materially adversely affect our business, financial condition and results of operations.

Even if the FDA or EMEA 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 or EMEA 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.

If our Phase III clinical trial is unsuccessful or we cannot produce comparable drug product, have not correctly understood the regulatory requirements associated with comparability of drug products or for various other reasons cannot satisfy ongoing regulatory requirements, we may not receive NDA and/or MAA approvals or such approvals may be substantially delayed or withdrawn. Any of these events could materially adversely affect our business, financial condition and results of operations.

We cannot be certain that we will obtain any regulatory approvals in foreign countries. 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 U.S. and European Union (E.U.) territories, our corporate partners and we must comply with numerous and varying regulatory requirements of other countries. The approval procedures vary among countries and can involve additional product testing and administrative review periods. The time required to obtain approval in these other territories might differ from that required to obtain FDA or EMEA approval. The regulatory approval process in these other territories includes at least all of the risks associated with obtaining FDA and EMEA approval detailed above. Approval by the FDA or EMEA does not ensure approval by the regulatory authorities of other countries.

We are currently conducting or planning to conduct several clinical studies in the U.S., E.U. and other territories with our products. If we are unable to receive regulatory approval to conduct such studies, it may prevent or substantially delay our development programs which could materially adversely affect our business, financial condition and results of operations.

If another party obtains orphan drug or pediatric exclusivity for a product that is essentially the same as rhIGF-I/rhIGFBP-3 for the treatment of growth disturbance due to GHIS, we may be precluded or delayed from commercializing rhIGF-I/rhIGFBP-3 in that indication. This will materially adversely affect our business, financial condition and results of operations.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. The company that obtains the first marketing approval from the FDA for a designated orphan drug for a rare disease receives marketing exclusivity for use of that drug for the designated condition for a period of seven years. Similar laws exist in Europe. Pediatric exclusivity can provide an additional six months of market exclusivity in the U.S. If a competitor obtains approval of the same drug for the same indication or disease before us, we would be blocked from obtaining approval for our product for seven or more years, unless our product can be shown to be clinically superior. In addition, more than one product may be approved by the FDA for the same orphan indication or disease as long as the products are different drugs. As a result, if our product is approved and receives orphan drug status, the FDA can still approve other drugs for use in treating the same indication or disease covered by our product, which could create a more competitive market for us.

We are aware of a drug being developed by Tercica, Inc., which we believe is a product containing essentially only rhIGF-I, that is in development for treatment of Severe Pediatric IGF-I Deficiency. We believe this population includes patients with GHIS. We believe this company has or will file for orphan designation of their product and pursue pediatric exclusivity. The regulatory agencies could determine that this other product is the same drug as our product and is used for the same indication. If the regulatory agencies make this determination and the other product is approved first, the approval of our rhIGF-I/rhIGFBP-3 for GHIS could be blocked for up to seven or more years, which could force us to curtail or cease our operations. We may not be able to benefit from the orphan drug marketing exclusivity because products that are clinically superior may be approved for marketing regardless of whether we receive orphan drug designation and the first marketing approval.

The failure to successfully obtain orphan drug market exclusivity or pediatric drug market exclusivity will adversely affect our business, financial condition and results of operations.

Manufacturing capacity necessary to supply rhIGF-I/rhIGFBP-3 and rhIGFBP-3 may not be available, which may adversely affect our business, financial condition and results of operations. If we are unable to find sufficient manufacturing capacity, it could materially adversely affect our business, financial condition and results of operations.

We have no internal manufacturing capability. Failure to successfully manufacture our products could materially adversely affect our business, financial condition and results of operations. We intend to enter into strategic alliances with other parties that have established commercial scale manufacturing capabilities. There can be no assurance that we will enter into 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 pre-clinical and clinical trials may be adversely affected. In addition, there can be no assurance that an adverse regulatory 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 be time consuming, resource intensive and capital intensive. If our contract manufacturers' facilities or we can not produce our products according to current good manufacturing practices (cGMP) and pass a cGMP inspection or

if our contract manufacturers' or our facilities become unavailable, we may be unable to develop and commercialize our products. This will materially adversely affect our business, financial condition and results of operations.

The available capacity for the manufacture of recombinant proteins that comprise rhIGF-I/rhIGFBP-3 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.

We have signed an agreement with Avecia Limited to manufacture rhIGF-I/rhIGFBP-3 at Avecia's site at Billingham, England. At present, rhIGF-I/rhIGFBP-3 has never been manufactured by Avecia at scales necessary for Phase III and commercialization; we cannot guarantee that they will be able to produce rhIGF-I/rhIGFBP-3 at scales necessary for Phase III and commercialization or that there will not be delays in such production. If we are unable to manufacture rhIGF-I/rhIGFBP-3 or such manufacture is delayed it could materially adversely affect our business, financial condition and results of operations.

The facilities used by our contract manufacturers, including Avecia Limited, to manufacture rhIGF-I/ rhIGFBP-3 may undergo an inspection by the FDA and/or EMEA for compliance with cGMP regulations, before rhIGF-I/rhIGFBP-3 can be approved. In the event these facilities do not receive a satisfactory cGMP inspection for the manufacture of our product, we may need to fund additional modifications to our manufacturing process, conduct additional validation studies, or find alternative manufacturing facilities, any of which would result in significant cost to us as well as a significant delay of up to several years in obtaining approval for rhIGF-I/ rhIGFBP-3. In addition, our contract manufacturers, and any alternative contract manufacturer we may utilize, will be subject to ongoing periodic inspection by the FDA and EMEA and other foreign agencies for compliance with cGMP regulations and similar foreign standards. We do not have control over our contract manufacturers' compliance with these regulations and standards.

Currently, Avecia Limited is our sole provider of bulk rhIGF-I/rhIGFBP-3. We have no alternative manufacturing facilities. If Avecia Limited's facilities or any of our other contract manufacturers' facilities become unavailable to us for any reason, including failure to comply with cGMP regulations, damage from any event, including fire, flood, earthquake, or terrorism or if they fail to perform under our agreement with them, we may be unable to complete manufacture of rhIGF-I/rhIGFBP-3 or validation of the manufacturing process for rhIGF-I/rhIGFBP-3. This could delay our clinical trials and the approval of our NDA or MAA, which would delay or otherwise adversely affect revenues. If the damage to any of these facilities is extensive, or, for any reason, they do not operate in compliance with cGMP or are unable or refuse to perform under our agreements, we will need to find alternative facilities. The number of contract manufacturers with the expertise and facilities to manufacture rhIGF-I/rhIGFBP-3 bulk drug substance on a commercial scale in accordance with cGMP regulations is extremely limited, and it would take a significant amount of time to arrange for alternative manufacturers. If we need to change to other commercial manufacturers, we would need to transfer and validate the processes and analytical methods necessary for the production and testing of rhIGF-I/rhIGFBP-3 to these new manufacturers. Any of these factors could lead to the delay or suspension of our clinical trials, regulatory submissions, regulatory approvals or commercialization of rhIGF-I/rhIGFBP-3, or higher costs of production and result in our failure to effectively commercialize rhIGF-I/rhIGFBP-3.

Furthermore, if our contract manufacturers fail to deliver commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, and we are unable to promptly find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volume and on a timely basis, we will likely be unable to meet demand for rhIGF-I/rhIGFBP-3 and we would lose potential revenues.

We currently have limited sales, marketing and distribution capabilities, which may make commercializing our products difficult. If we are unable to build sales, marketing and distribution capabilities, it will materially adversely affect our business, financial condition and results of operations.

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. Failure to successfully sell, market or distribute our products once approved will materially adversely affect our business, financial condition and results of operations

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 and future treatment methods;
- their price; and
- reimbursement policies of government and third-party payers, including hospitals and 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.

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 payers' 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.

If physicians, patients, third-party payers or the medical community in general do not accept and use the products we develop and commercialize, it will materially adversely affect our business, financial condition and results of operations.

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 execute our business plan. Our future capital requirements will depend on many factors, including factors associated with:

- manufacturing;
- process development;
- research and development including among other items, pre-clinical testing and clinical trials;
- obtaining regulatory approvals;
- obtaining marketing sales and distribution capabilities;
- launching products;
- retaining employees and consultants;
- filing and prosecuting patent applications and enforcing patent claims;
- establishing strategic alliances; and
- other activities required for product commercialization.

We may also need to spend more money than currently expected because we may change our product development plans, acquire additional products or product candidates or we may misjudge our costs. We have no committed sources of capital and do not know whether additional financing will be available when needed, or, if available, that the terms will be favorable. 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. We believe that existing cash reserves will sufficiently fund our activities through the next twelve months.

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. This may 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 depend highly 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, manufacturing, sales, marketing and distribution 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 our business, financial condition and results of operations.

We need collaborative relationships to be successful. If we are unable to form these relationships it could adversely impact our business, financial condition and results of operations.

We currently rely and may in the future rely on a number of significant collaborative relationships for intellectual property rights, research funding, manufacturing, analytical services, pre-clinical development, 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, licensed to or licensed from corporate partners;
- disagreements with corporate partners could result in loss of intellectual property rights, 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, impair or prevent the development and commercialization of our products and 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 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.

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 rhIGF-I and/or rhIGFBP-3. 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 rhIGF-I/rhIGFBP-3 or rhIGFBP-3. 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, Amgen, Novartis AG, and Robert Rieveley hold United States and/or foreign patents possibly directed to the composition, production and/or use of rhIGF-I, rhIGFBP-3, rhIGF-I/rhIGFBP-3 and/or recombinant proteins in general. After examining these patents, we do not believe they present an obstacle to our plans to commercialize rhIGF-I/rhIGFBP-3 and rhIGFBP-3. However, we can provide no assurance that any one of these third parties will not assert in the future a contrary position, for instance in the

context of an infringement action. Moreover, while we cannot predict with certainty the outcome of such a proceeding, an adverse ruling could impact our ability to make, use or sell our products.

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.

In 1998 Genentech requested a hearing with the European Patent Office to oppose the validity of one of our European patents with claims to rhIGFBP-3, uses of rhIGFBP-3 and uses of rhIGF-I/rhIGFBP-3. As of yet, no hearing date has been set by the European Patent Office. Should the opposition hearing be held and should Genentech prevail, some or all of the claims of this patent may be revoked. This result could lessen our ability to exclude others, but would not affect our own ability, to practice these claims.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information. Disclosure of this information may materially adversely affect our business, financial condition and results of operations.

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 will materially adversely affect 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.

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, among others, will determine our ability to compete effectively:

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

Currently, no drug in the U.S. or Europe is approved and marketed as replacement therapy for the treatment of GHIS. Other than Insmed, we are aware of only one other company, Tercica, Inc., that is pursuing development of a product for this indication or a similar indication. Tercica, in documents filed with the Securities and Exchange Commission, has stated that it plans to submit a NDA for the use of rhIGF-I in the treatment of severe pediatric IGF-I deficiency in 2005. We believe this indication would include patients with GHIS. We believe Tercica may also be planning to develop rhIGF-I for some of the same indications that we plan to pursue with rhIGF-I/rhIGFBP-3.

Growth hormone may also be a competitive product for the treatment of some indications that we may pursue with rhIGF-I/rhIGFBP-3. The major suppliers of commercially available growth hormone are Genentech, Eli Lilly, Novo Nordisk, Pfizer and Serono. We believe that Novo Nordisk may be conducting clinical trials for the use of its growth hormone in pediatric IGF-I deficiency. We are also aware that Serono is conducting a Phase III trial with growth hormone for the treatment of HIV associated adipose redistribution syndrome.

In addition, we believe that Genentech, Merck, Novo Nordisk and Pfizer have previously conducted research and development of orally-available small molecules that cause the release of growth hormone, known as growth hormone secretagogues. We are not aware of any continued clinical development of these molecules by these companies. We believe that Rejuvenon Corporation may have licensed certain rights to Novo Nordisk's growth hormone secretagogues, which are in pre-clinical development. We are also aware that Theratechnologies is developing various peptides that stimulate the release of hormones that could be used in the treatment of some of the same indications we plan to pursue with rhIGF-I/rhIGFBP-3.

Many companies are seeking to develop products and therapies for the treatment of diabetes. Our competitors include multinational pharmaceutical companies, specialized biotechnology firms, and universities and other research institutions. Our largest competitors include Amylin Pharmaceuticals, Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, Merck, Novartis, Novo Nordisk and Takeda Chemical Industries. Various products are currently available to treat type 2 diabetes, such as insulin and oral hypoglycemic drugs.

In addition, several companies are developing various new approaches to improve the treatments of type 1 and type 2 diabetes. Specifically, Amylin Pharmaceuticals has conducted and is continuing to conduct clinical trials for two products, Symlin and Exenatide, for the treatment of type 2 diabetes. Tercica has indicated that it plans to pursue the development of rhIGF-I in the treatment of severe forms of diabetes.

Many companies are pursuing the development of products for the treatment of cancer. Our competitors include multinational pharmaceutical companies, specialized biotechnology firms, and universities and other research institutions. Although we are unaware of any companies developing rhIGFBP-3 for cancer we are aware of companies who are developing products that are intended to target the same pathway as rhIGFBP-3.

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.

Our inability to compete in our industry could materially adversely affect our business, financial condition and results of operations.

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, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

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:

- our listing status on the Nasdaq National Market;
- results of our clinical trials and pre-clinical 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. 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.

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

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

Certain provisions of Virginia law, our articles of incorporation and our amended and restated bylaws, and our Stockholder Rights Plan make a hostile 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.

Available Information and Corporate Governance Documents.

Our Internet website address is: www.insmed.com. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after such documents are electronically filed with, or furnished to, the SEC. In addition, our Corporate Governance Guidelines, Code of Business Conduct and Ethics, and the charters of our Audit, Compensation and Nominating of Governance Committees are available on our website and are available in print, without charge, to any shareholder upon written request by writing our Treasurer and Controller at 4851 Lake Brook Drive, Glen Allen, Virginia 23060. The information on our website is not, and shall not be deemed to be, a part of this report or incorporated into any other filings we make with the SEC.

ITEM 2. PROPERTIES

We occupy 46,000 square feet of office and laboratory space in Glen Allen, Virginia. Our annual cash cost for the space including utilities and services in 2004 are approximately $1.1 million 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, 2003.

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER REPURCHASES OF EQUITY SECURITIES

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. On January 22, 2003, Insmed received a NASDAQ Staff Determination indicating that the Company has failed to comply with NASDAQ's minimum bid price requirement of $1.00 per share for continued listing of the Company's common stock on the NASDAQ National Market as set forth in Marketplace Rule 4450(a)(5). As a result, the Company's common stock was subject to delisting from the NASDAQ National Market on January 31, 2003. Following procedures set forth in the NASDAQ Marketplace Rule 4800 series, the Company requested a hearing before a NASDAQ Listing Qualifications Panel (the Panel) to review the Staff Determination. The hearing occurred on March 6, 2003 and the delisting action was stayed pending the Panel's decision. On March 31, 2003, the Panel granted us continued listing on the Nasdaq National Market pursuant to an exception to the NASDAQ Marketplace Rules. On May 9, 2003, we received a letter from the Panel stating that the Panel had determined to continue the listing of our common stock on the Nasdaq National Market and that the hearing file had been closed.

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 National Market.

	Insmed Common Stock	
Fiscal Year 2003	High	Low
Fourth Quarter	$3.40	$2.50
Third Quarter	3.74	1.96
Second Quarter	3.56	0.60
First Quarter	0.65	0.39
Fiscal Year 2002	High	Low
Fourth Quarter	$0.73	$0.32
Third Quarter	2.00	0.37
Second Quarter	3.10	1.24
First Quarter	3.99	2.51

On February 27, 2004, the last reported sale price for our common stock on the Nasdaq National Market was $3.37 per share. As of February 27, 2004, there were 539 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, 2003. 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, 2003 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 31 to 35.

	Year Ended December 31, (numbers in thousand, except per share data)				
	1999	2000	2001	2002	2003
Historical Statement of Operations Data:					
Revenues	$ —	$ 60	$ 296	$ 1,955	$ 150
Operating expenses:					
Research and development	5,657	21,608	35,506	18,077	7,140
General and administrative	2,189	5,989	4,881	2,984	3,477
Operational restructuring charge	—	—	—	2,533	—
Goodwill impairment charge	—	—	—	15,385	—
Purchased research and development	—	50,434	—	—	—
Stock compensation	285	3,564	95	—	119
Total operating expenses	8,131	81,595	40,482	38,979	10,736
Operating loss	(8,131)	(81,535)	(40,186)	(37,024)	(10,586)
Interest income, net	338	1,873	3,017	607	288
Loss before income taxes	(7,793)	(79,662)	(37,169)	(36,417)	(10,298)
Income tax expense	—	200	—	—	—
Net loss	(7,793)	(79,862)	(37,169)	(36,417)	(10,298)
Basic and diluted net loss per share	(2.47)	(4.36)	(1.13)	(1.10)	(0.29)
Weighted average shares	3,155	18,319	32,871	33,066	35,600
Historical Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 4,635	$ 83,083	$ 51,250	$ 27,337	$ 29,526
Total assets	5,296	102,718	71,606	28,308	29,812
Stockholders' equity	4,462	96,782	59,695	23,448	26,220

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 metabolic and endocrine disorders. We have two lead drug candidates—rhIGF-I/rhIGFBP-3 and rhIGFBP-3.

We have not been profitable and have accumulated deficits of approximately $186.5 million through December 31, 2003. 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 may increase as development of our product candidates progresses. However, there will be fluctuations from period to period caused by differences in project costs incurred at each stage of development.

The full cost and completion dates, through commercialization, of our current research and development projects, rhIGF-I/rhIGFBP-3 and rhIGFBP-3, are entirely dependent on the results of our current Phase II and Phase III clinical trials, potential future clinical trials for rhIGF-I/rhIGFBP-3, the subsequent review of the Phase III results with the FDA, and our pre-clinical trials with rhIGFBP-3. 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, 2003 compared to Year Ended December 31, 2002

For the year ended December 31, 2003, we recorded a net loss of $10.3 million. Research and development expenses (which 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) decreased $11.0 million from $18.1 million in 2002 to $7.1 million in 2003 as a result of decreased clinical trial activity.

Clinical and contract manufacturing costs related to the development of rhIGF-I/rhIGFBP-3 decreased approximately $0.3 million from $3.5 million in 2002, to $3.2 million in 2003 as we completed the development phase and began to scale up our production process for rhIGF-I/rhIGFBP-3 and rhIGFBP-3 with our contract manufacturer, Avecia.

General and administrative expenses increased $0.5 million from $3.0 million for 2002 to $3.5 million for 2003. The increase, although seen across all support services, is primarily due to higher external service costs.

In the third quarter of 2002, we recorded a restructuring charge of $2.5 million related to the previously announced discontinuation of our INS-1 development program. The components of this charge include expenses of $1.2 million related to the anticipated payouts under lease agreements for laboratory space no longer utilized at our headquarters, $0.7 million related to the impairment of idle laboratory equipment at our headquarters, and $0.6 million related to the cost of severance benefits following the termination of approximately 55% of our workforce. We also recorded a $15.4 million goodwill write-off in the fourth quarter of 2002 relating to the Celtrix acquisition in 2000.

Revenues decreased $1.8 million from $2.0 million in 2002 to $0.2 million in 2003. The decrease in revenues as compared with 2002 is due to the recognition of approximately $1.7 million of revenue from an international license fee for INS-1 from Taisho Pharmaceutical Co., Ltd. This represents revenues, previously

deferred, from a cash payment made by Taisho at the inception of the Joint Development Agreement with us in 2000, which was being recognized as revenue over the life of the corresponding patent. As Taisho announced the termination of this agreement, the balance of the unrecognized revenue was recorded in the third quarter of 2002.

As of December 31, 2003, cash and cash equivalents increased to $29.5 million from $27.3 million at December 31, 2002. As a result of a lower average cash balance and lower interest rates in 2003 compared to 2002, net interest income decreased $0.3 million from $0.6 million in 2002 to $0.3 million in 2003.

Accounts payable and accrued project costs decreased $0.8 million from $3.2 million at December 31, 2002 to $2.4 million at December 31, 2003 as a result of decreased clinical and manufacturing activity. Stockholders' equity increased $2.8 as a result of approximately $13.0 million in proceeds received by us in connection with a private placement of our common stock on July 15, 2003, net of the loss in 2003. The accumulated deficit at December 31, 2003 increased to approximately $186.5 million due to our 2003 net loss of $10.3 million.

Year Ended December 31, 2002 compared to Year Ended December 31, 2001

For the year ended December 31, 2002, we recorded a net loss of $36.4 million. Research and development expenses (which 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) decreased $17.4 million from $35.5 million in 2001 to $18.1 million in 2002 as a result of decreased clinical trial activity. INS-1 expenses decreased $15.1 million during 2002, compared to 2001, as follows:

- Amounts paid to contract research organizations and for site grants, monitoring and other clinical trial-related costs decreased approximately $12.6 million from $17.8 million in 2001 to $5.2 million in 2002. This decrease was primarily due to the winding down of the INS-1 Phase II clinical trials.
- Contract manufacturing costs to supply INS-1 for our trials decreased $2.5 million from $4.2 million in 2001 to $1.7 million in 2002. This decrease was primarily due to the supply buildup of the INS-1 drug in 2001 and the subsequent use of that drug in 2002.

Clinical and contract manufacturing costs related to the development of rhIGF-I/rhIGFBP-3 decreased approximately $6.2 million, to $3.8 million in 2002 as we completed the development phase and began to scale up our production process for rhIGF-I/rhIGFBP-3 and rhIGFBP-3 with our contract manufacturer, Avecia.

General and administrative expenses decreased $1.9 million from $4.9 million for 2001 to $3.0 million for 2002. The decrease, although seen across all support services, was primarily due to lower shareholder expenses, legal fees and accounting services.

In the third quarter of 2002, we recorded a restructuring charge of $2.5 million related to the previously announced discontinuation of our INS-1 development program. The components of this charge include expenses of $1.2 million related to the anticipated payouts under lease agreements for laboratory space no longer utilized at our headquarters, $0.7 million related to the impairment of idle laboratory equipment at our headquarters, and $0.6 million related to the cost of severance benefits following the termination of approximately 55% of our workforce.

We also recorded a $15.4 million goodwill write-off in the fourth quarter of 2002 relating to the Celtrix acquisition in 2000. In accordance with Statement of Financial Accounting Standards (SFAS) No. 142, we tested the goodwill being carried on our balance sheet relating to the Celtrix acquisition for impairment by comparing the carrying amount of our net assets to our fair value. In accordance with Generally Accepted Accounting Principles (GAAP), we adopted the current market value of our stock as the basis for supporting the fair value of our net assets. On this basis, we determined that there had been impairment to the goodwill and the entire remaining amount of unamortized goodwill of $15.4 million was written off.

Revenues increased $1.7 million from $0.3 million in 2001 to $2.0 million in 2002. The increase in revenues as compared with 2001 is due to the recognition of approximately $1.7 million of revenue from Taisho Pharmaceutical Co., Ltd. This represents revenues, previously deferred, from a cash payment made by Taisho at the inception of the Joint Development Agreement with us in 2000, which were being recognized as revenue over the life of the corresponding patent. As Taisho announced the termination of this agreement, the balance of the unrecognized revenue was recorded in the third quarter of 2002.

As of December 31, 2002, cash and cash equivalents decreased to $27.3 million from $51.3 million at December 31, 2001. As a result of a lower average cash balance in 2002 compared to 2001, net interest income decreased $2.4 million from $3.0 million in 2001 to $0.6 million in 2002. Net receivables from Taisho for its portion of certain INS-1 development activities decreased $3.3 million from $3.5 million as of December 31, 2001, to $0.2 million as of December 31, 2002.

Accounts payable and accrued project costs decreased $6.2 million from $9.4 million at December 31, 2001 to $3.2 million at December 31, 2002 as a result of decreased clinical and manufacturing activity. Stockholders' equity decreased $36.3 as a result of the net loss in 2002, net of stock option exercises. The accumulated deficit at December 31, 2002 increased to approximately $176.2 million due to our 2002 net loss of $36.4 million.

Liquidity and Capital Resources

At December 31, 2003, our cash and cash investments were approximately $29.5 million and were invested in money market instruments. We believe that our current cash position will be sufficient to fund our operations through the next twelve months.

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.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources that we believe is material to investors.

Contractual Obligations

We are obligated to make future payments under various contracts as set forth below:

	Payments due by period (in thousands)		
Contractual Obligations	Total	Less than 1 year	1-3 years
Operating Lease Obligations	$2,080	$ 797	$1,283
Purchase Obligations	1,445	1,445	—
Total	$3,525	$2,242	$1,283

Critical Accounting Policies

In Management's Discussion and Analysis, we discuss the results of operations and financial condition as reflected in the our consolidated financial statements, which have been prepared in accordance with GAAP.

Preparation of financial statements requires us to make estimates and assumptions affecting the reported amounts of assets, liabilities, revenues and expenses and the disclosures of contingent assets and liabilities. We use our historical experience and other relevant factors when developing our estimates and assumptions. We continually evaluate these estimates and assumptions. Note 1 to the Company's consolidated financial statements includes a discussion of our significant accounting policies. The accounting policies discussed below are those we consider critical to an understanding of our consolidated financial statements because their application places the most significant demands on our judgment. Our financial results might have been different if different assumptions had been used or other conditions had prevailed.

Stock-Based Compensation

We recognize 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,* as amended by FASB Statement No. 148, *Accounting for Stock-Based Compensation – Transition and Disclosure*, are presented in Notes 1 and 3. The fair value for these awards was estimated at the date of grant using the Black-Scholes pricing method assuming a weighted average volatility, a risk-free interest rate, no dividends, and a weighted-average expected life of the option.

Stock options granted to non-employees are accounted for in accordance with the Emerging Issues Task Force (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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We invest excess cash in investment grade, interest-bearing securities and, at December 31, 2003, had $29.5 million invested in money market instruments. Such investments are subject to interest rate and credit risk. Our policy of investing in highly rated securities whose maturities, at December 31, 2003, are all less than 3 months minimizes such risks. In addition, while a hypothetical 1.0% per annum decrease in market interest rates would reduce interest income in 2004, 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-13.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Pursuant to Rule 13a-15(b) under the Securities and Exchange Act of 1934, we carried out an evaluation, with the participation of our management, including the Chairman of the Board and Chief Executive Officer and Treasurer and Controller, of the effectiveness of our disclosure on controls and procedures (as defined under Rule 13a-15(e) under the Securities Exchange Act of 1934) as of the end of the period covered by this report. Based upon that evaluation, our Chairman of the Board and Chief Executive Officer and Treasurer and Controller concluded that our disclosure controls and procedures are effective in timely alerting them to material information relating to Insmed (including its consolidated subsidiaries) required to be included in our periodic SEC filings.

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2003, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information presented under the captions "Nominees," "Directors Whose Terms Expire at the 2005 Annual Meeting (Class II Directors)," "Directors Whose Terms Expire at the 2006 Annual Meeting (Class III Directors)," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Meetings of the Board and its Committees – Audit Committee" of the Company's definitive Proxy Statement for the 2004 Annual Meeting of Shareholders (the "2004 Proxy Statement") is incorporated herein by reference. Such 2004 Proxy Statement will be filed with the Securities and Exchange Commission in April 2004.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees (including our President and Chief Executive Officer and our Treasurer and Controller) and have posted the Code of Business Conduct and Ethics on our website. We intend to satisfy the disclosure requirement under Item 10 of Form 8-K relating to amendments to or waivers from any provision of our Code of Business Conduct and Ethics applicable to our President and Chief Executive Officer and our Treasurer and Controller by posting this information on our website. Our Internet website address is www.insmed.com. The information on our website is not, and shall not be deemed to be, part of this report or incorporated into any other filings we make with the SEC.

ITEM 11. EXECUTIVE COMPENSATION

The information presented under the captions "Executive Officer Compensation" and "Director Compensation" of the 2004 Proxy Statement is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information presented under the captions "Stock Ownership" and "Equity Compensation Plan Information" of the 2004 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 2004 Proxy Statement is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information presented under the captions "Fees Paid to Ernst & Young LLP" and "Audit Committee Pre-Approval Policy" of the Audit Committee Report included in the 2004 Proxy Statement is incorporated herein by reference.

PART IV

ITEM 15. 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 Statements 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, 10.2 and 10.17 constitute management contracts or compensatory plans or arrangements required to be filed as exhibits hereto.

(b) Reports on Form 8-K.

A report on Form 8-K (Items 7 and 12), dated November 5, 2003, was furnished to report that the Insmed Incorporated issued a press release announcing its financial position, result of operations and cash flows for the three-month and nine-month periods ended September 30, 2003 (not incorporated by reference).

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 12th day of March, 2004.

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 12th day of March, 2004.

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 C.G.A.	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/ 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, 2003 and 2002 and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2003. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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, 2003 and 2002, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2003, in conformity with accounting principles generally accepted in the United States.

As discussed in Note 1 to the financial statements, in 2002 the Company changed its method for accounting for goodwill and other intangible assets to comply with the accounting provisions of Statement of Financial Accounting Standards No. 142.

/s/ Ernst & Young LLP

McLean, Virginia
January 22, 2004

INSMED INCORPORATED

CONSOLIDATED BALANCE SHEETS
(in thousands)

	December 31, 2003	2002
ASSETS		
Current assets:		
Cash and cash equivalents	$ 29,526	$ 27,337
Due from Taisho Pharmaceutical Co., Ltd.	—	199
Other current assets	225	615
Total current assets	29,751	28,151
Property and equipment, net	61	157
Total assets	$ 29,812	$ 28,308
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 660	$ 941
Accrued project costs	1,747	2,283
Payroll liabilities	205	358
Restructuring reserve	334	310
Total current liabilities	2,946	3,892
Restructuring reserve—long-term portion	646	968
Total liabilities	3,592	4,860
Stockholders' equity:		
Common stock, $.01 par value; authorized share 500,000,000; issued and outstanding shares, 38,394,994 in 2003 and 33,186,336 in 2002	384	332
Additional capital	212,362	199,344
Accumulated deficit	(186,526)	(176,228)
Net stockholders' equity	26,220	23,448
Total liabilities and stockholders' equity	$ 29,812	$ 28,308

See accompanying notes.

INSMED INCORPORATED

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

	Year Ended December 31, 2003	2002	2001
Revenues	$ 150	$ 1,955	$ 296
Operating expenses:			
Research and development	7,140	18,077	35,506
General and administrative	3,477	2,984	4,881
Operational restructuring charge	—	2,533	—
Goodwill impairment charge	—	15,385	—
Non-cash stock compensation	119	—	95
Total operating expenses	10,736	38,979	40,482
Operating loss	(10,586)	(37,024)	(40,186)
Interest income	288	607	3,017
Income tax expense	—	—	—
Net loss	$(10,298)	$(36,417)	$(37,169)
Basic and diluted net loss per share	$ (0.29)	$ (1.10)	$ (1.13)
Shares used in computing basic and diluted net loss per share	35,600	33,066	32,871

See accompanying notes.

INSMED INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
YEARS ENDED DECEMBER 31, 2003, 2002, AND 2001
(in thousands, except share amounts)

	Common Stock	Additional Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
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
Issuance of 198,282 shares of common stock upon exercise of stock options	2	125	—	—	127
Issuance of 56,289 shares of common stock from Employee Stock Purchase Plan	1	42	—	—	43
Comprehensive earnings:					
Net loss	—	—	(36,417)	—	(36,417)
Comprehensive loss	—	—	—	—	(36,417)
Balance at December 31, 2002	332	199,344	(176,228)	—	23,448
Issuance of 53,171 shares of common stock upon exercise of stock options	1	53	—	—	54
Issuance of 36,439 shares of common stock from Employee Stock Purchase Plan	—	27	—	—	27
Issuance of 5,146,846 shares of common stock and 1,544,046 warrants for cash, net of offering costs of $972,593	51	12,872	—	—	12,923
Stock issued for consulting services	1	118	—	—	119
Stock re-purchase from Taisho	(1)	(52)			(53)
Comprehensive earnings:					
Net loss	—	—	(10,298)	—	(10,298)
Comprehensive loss	—	—	—	—	(10,298)
Balance at December 31, 2003	$384	$212,362	$(186,526)	$ —	$ 26,220

See accompanying notes.

INSMED INCORPORATED

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2003	2002	2001
Operating activities			
Net loss	$(10,298)	$(36,417)	$(37,169)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	96	346	707
Amortization of goodwill	—	—	835
Goodwill impairment charge		15,385	—
Operational restructuring—non-cash	—	1,947	—
Recognition of deferred revenues	—	(1,798)	(143)
(Gain) loss on sale of marketable securities	—	—	(211)
Issuance of stock for services	119	—	95
Changes in operating assets and liabilities:			
Due from Taisho Pharmaceutical Co., Ltd.	199	3,322	(2,293)
Other assets	390	(337)	281
Accounts payable	(281)	(3,486)	1,810
Accrued project costs and other	(536)	(2,684)	4,193
Other liabilities	(153)	(361)	115
Restructuring reserve	(298)	—	—
Net cash used in operating activities	(10,762)	(24,083)	(31,780)
Investing activities			
Proceeds from marketable securities matured and sold	—	—	11,500
Purchases of property and equipment	—	—	(251)
Net cash provided by investing activities	—	—	11,249
Financing activities			
Proceeds from issuance of common stock	12,951	170	153
Net cash provided by financing activities	12,951	170	153
Increase (decrease) in cash and cash equivalents	2,189	(23,913)	(20,378)
Cash and cash equivalents at beginning of period	27,337	51,250	71,628
Cash and cash equivalents at end of period	$ 29,526	$ 27,337	$ 51,250

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. Abnormalities in the Growth Hormone (GH)/ Insulin-like Growth Factor I (IGF-I) axis often manifests in multiple endocrine and metabolic conditions, such as growth disorders. Additionally, other conditions such as diabetes are exacerbated by imbalances in the GH/ IGF-I axis. Insmed's cancer development program focuses on rhIGFBP-3, the primary binding protein of IGF-I. Insmed's rhIGFBP-3 technology may curtail abnormal cell growth by introducing an excess of rhIGFBP-3 to bind and regulate free IGF-I. Since rhIGFBP-3 interrupts the cell growth signal early in the sequence, rhIGFBP-3 is considered an upstream growth factor inhibitor.

Insmed has two lead drug candidates: rhIGF-I/rhIGFBP-3, which is expected to begin Phase III Clinical testing for GHIS in 2003, and rhIGFBP-3, which is currently undergoing Pre-Clinical trials in the oncology area. The Company is actively developing rhIGF-I/rhIGFBP-3 to treat GHIS and diabetes, and are concurrently continuing pre-clinical studies on rhIGFBP-3 in the cancer indication as an anti-tumor agent.

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.

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,	
	2003	2002
	(in thousands)	
Furniture and office equipment	$ 511	$ 511
	511	511
Accumulated depreciation	(450)	(354)
Property and equipment, net	$ 61	$ 157

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, accounts payable, and accrued expenses to approximate the fair value of the respective assets and liabilities at December 31, 2003 and 2002 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.

In accordance with FASB Statement No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure* ("SFAS 148"), the effect on net loss and net loss per share if the Company had applied the fair value recognition provisions of SFAS No. 123 to stock-based employee compensation is as follows:

Stock Compensation Expense
(in thousands, except per share data)

	Year Ended December 31,		
	2003	2002	2001
Net Loss	$(10,298)	$(36,417)	$(37,169)
Net Loss Per Share (Basic and Diluted)	$ (0.29)	$ (1.10)	$ (1.13)
Stock based employee compensation cost (under APB 25)	—	—	95
Pro-forma Fair value stock compensation expense	(2,001)	(2,731)	(2,222)
Pro-Forma Net Income	(13,131)	(39,148)	(39,391)
Pro-Forma Net Loss Per Share (Basic and Diluted)	$ (0.37)	$ (1.18)	$ (1.20)

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 127% in 2003, 106% in 2002, and 89% in 2001, a risk-free interest rate of 3.0% in 2003, 3.0% in 2002, and 4.5% in 2001, no dividends, and a weighted-average expected life of the option of 4.93 years in 2003, 5.7 years in 2002 and 5 years in 2001. Compensation expense for fixed awards with pro-rata vesting is recognized under the straight-line method.

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.*

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 2002, the FASB issued SFAS No. 146, *Accounting for Costs Associated with Exit or Disposal Activities*. This statement addresses financial accounting and reporting for costs associated with exit or disposal activities and nullifies Emerging Issues Task Force (EITF) Issue No. 94-3, *Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (including Certain Costs Incurred in a Restructuring)*. The statement is effective for exit or disposal activities initiated after December 31, 2002. the adoption of this pronouncement did not have an impact on the Company's financial statements.

In January 2003, the Financial Accounting Standard Board (FASB) issued FASB Interpretation 46, *Consolidation of Variable Interest Entities* (the "Interpretation") . In general, the Interpretation requires that the assets, liabilities, and activities of a Variable Interest Entity ("VIE") be consolidated into the financial statements of the enterprise that has the controlling financial interest. Companies with VIEs that existed prior to the issuance of the Interpretation will be required to apply the guidance to existing VIEs for the first fiscal period ending after March 15, 2004. The consolidation requirement of FASB Statement No. 46 are effective immediately for any VIE's that were established subsequent to February 1, 2003. The adoption of the interpretation did not have an impact on the Company's financial statements.

2. Operational Restructuring

On September 10, 2002, the Company announced that it would immediately discontinue the internal development of one of its investigational drug candidates, INS-1, based on the results of recently completed Phase II clinical trials. Similarly, the Company's Japanese partner to develop INS-1 in Japan and Asia, Taisho, also indicated its intention to discontinue its involvement in any future development in INS-1, and terminated the joint development agreement in accordance with the terms of the agreement.

As a result of the decision to discontinue the INS-1 development program and Taisho's notice to terminate the joint development agreement, the Company approved a restructuring plan to focus on its remaining drug candidates. In the third quarter of 2002, the Company recorded a restructuring charge of $2.5 million. The components of the restructuring charge included expenses of $1.2 million related to the anticipated payouts under lease agreements for laboratory space no longer utilized at the Company's headquarters, $0.6 million related to the impairment of idle laboratory equipment at the Company's headquarters, and $0.6 million related to the cost of severance benefits after the termination of 32 employees, or 55% of the workforce, at the Company's headquarters and laboratory in Glen Allen, Virginia. At December 31, 2003, approximately $0.3 million and $0.7 million of these costs remain accrued in the current and long-term portions of the restructuring reserve, respectively. These balances are expected to closely approximate the remaining costs to be incurred by the Company for lease obligations. Lease termination costs are anticipated to extend through 2006.

As a result of Taisho's decision to terminate the joint development agreement, the Company also recognized revenue from the Taisho agreement totaling $1.7 million. This item represents revenues previously deferred from a cash payment made by Taisho at inception of the joint development agreement that was being recognized as revenue over the estimated life of the corresponding agreement. Due to the termination of the agreement, the balance of the deferred revenue was recognized in 2002.

3. Stockholders' Equity

Common Stock

On July 15, 2003 Insmed Incorporated concluded a private placement of 5,146,846 shares of common stock to a group of institutional investors at a price of $2.70 per share, raising a total of approximately $13.9 million. The placement agent in the transaction received approximately $868,000 in fees and expenses (including fees paid to the placement agent's attorneys) resulting in net proceeds to the Company of approximately $13 million. The Company also issued warrants to purchase an additional 1,544,046 shares of common stock with an exercise price of $4.10 per share.

Periodically, the Company has issued shares of common stock in exchange for services provided by shareholders 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

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 maximum number of shares issuable under the plan is 6,250,000. 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 2003, 2002, and 2001 was $1.72, $1.36 and $3.37, respectively. A summary of stock option activity is as follows:

Description	2003	Weighted Average Exercise Price	2002	Weighted Average Exercise Price	2001	Weighted Average Exercise Price
Options outstanding at January 1	3,250,227	$4.49	3,143,561	$6.11	1,701,735	$7.39
Granted	1,349,000	1.72	1,984,750	1.98	1,812,465	4.66
Exercised	(53,171)	1.01	(198,282)	0.64	(115,962)	0.81
Cancelled	(645,540)	1.59	(1,679,802)	5.01	(254,677)	6.75
Options outstanding at December 31	3,900,516	$4.06	3,250,227	$4.49	3,143,561	$6.11

The following table summarizes options outstanding at December 31, 2003:

	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	471,901	5.96	0.61	250,895	0.71
$ 1.38 – $ 4.88	2,515,006	6.13	2.70	681,628	3.23
$ 5.000 – $ 8.25	463,220	5.14	6.20	355,674	6.20
$10.000 – $13.063	138,125	5.86	11.40	132,500	11.35
$13.313 – $14.00	309,375	2.61	13.67	232,032	13.67
$32.116	2,889	3.25	32.12	2,889	32.12
	3,900,516	5.70	4.06	1,655,618	5.65

A total of 8,044,046 shares of common stock were reserved at December 31, 2003 in connection with stock options, stock warrants, and the employee stock purchase plan.

4. Income Taxes

The deferred tax assets of approximately $93.8 million and $94.4 million at December 31, 2003 and 2002, 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, 2003 and 2002, the Company had net operating loss carryforwards for income tax purposes of approximately $232.8 million and $222.1 million, respectively, expiring in various years beginning in 2004. Utilization of these carryforwards will be significantly limited due to changes in the ownership of the Company's common stock.

Deferred tax assets (liabilities) consist of the following at December 31:

	2003	2002
	(in thousands)	
Deferred tax assets		
General Business Credits	4,224	8,810
Other	1,174	1,383
NOL Carryforwards	88,385	84,343
Total deferred tax assets	93,783	94,536
Deferred tax liabilities		
Other	(2)	(109)
Total deferred tax liabilities	(2)	(109)
Tax deferred asset/(liability)	93,781	94,427
Valuation allowance	(93,781)	(94,427)
Net deferred tax asset/(liability)	—	—

The differences between the U.S. federal statutory tax rate and the Company's effective tax rate are as follows:

	2003	2002
Statutory federal tax rate	34%	34%
State income taxes net of federal benefit	4	2
Research and development credit	(45)	12
Other	1	(14)
Change in valuation allowance	6	(34)
Total Expense	0%	0%

5. Leases

The Company leases office and laboratory space under an operating lease agreement expiring in October 2006. The lease provides for monthly rent of approximately $30,500 for the office space and $28,000 for the lab space with a 1.75% escalation per year. With the discontinuation of INS-1 and subsequent abandonment of the lab space, the company recognized $1.2 million of restructuring charge relating to this lease during the third quarter of 2002. The Company also leases a vehicle and office equipment. Future minimum payments on these leases at December 31, 2003 approximate $762,000, $772,000, and $571,000 in 2004, 2005, and 2006, respectively. Rent expense for all operating leases approximated $535,000 in 2003, $702,000 in 2002, and $663,000 in 2001.

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, 2003 there were 250,000 shares authorized for issuance under the plan and 111,131 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 401(k) 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 included 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 also funded 20% of the development costs for INS-1 in North America and Europe. Development costs reimbursable by Taisho approximated $1.6 million, $6.0 million and $2.3 million in 2002, 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 was previously being amortized into revenue, on a straight-line basis, over the estimated life of the corresponding patents. In addition, Taisho purchased 93,413 shares of the Company's common stock in 2000. In September 2003, Taisho indicated its intention to discontinue its involvement in any future development in INS-1, and terminated the joint development agreement in accordance with the terms of the agreement. As a result of this termination the Company recognized the remaining amount of the deferred license fee of $1.7 million in the 2002. In April of 2003 the Company repurchased the 93,413 shares of Insmed stock that was being held by Taisho.

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.

Pharmacia

In October 2002 we entered into an agreement with Pharmacia that grants us an exclusive license to Pharmacias portfolio of regulatory filings pertaining to rhIGF-I. In consideration for the exclusive license we have agreed to make therapy available to the 17 Growth Hormone Insensitivity Syndrome, (GHIS), subjects that were previously being treated with rhIGF-I supplied by Pharmacia.

Fujisawa Pharmaceutical Co., Ltd.

In January 2004, Insmed was granted a non-exclusive license to patent rights pertaining to the use of IGF-I therapy for the treatment of extreme or severe insulin resistant diabetes from Fujisawa Pharmaceutical Co., Ltd. Under the terms of the agreement, Insmed will obtain worldwide rights in territories (excluding Japan) where a valid patent claim exists, including the United States and Europe. We have made a commitment to use reasonable commercial efforts to make rhIGF-I/rhIGFBP-3 available on a named patient basis to patients with extreme insulin resistance.

Avecia Limited

In May 2002, we entered into an agreement with Avecia Limited, Europe's largest privately held specialty chemical company, for the process development and manufacture of rhIGF-I/rhIGFBP-3 In consideration for this process development and manufacturing agreement, we are obligated to pay success fees for process development milestones and manufacturing costs associated with ongoing production of rhIGF-I/rhIGFBP-3 and rhIGFBP-3.

8. Quarterly Financial Data (Unaudited)

	Fiscal Quarter							
	First		Second		Third		Fourth	
	2003	2002	2003	2002	2003	2002	2003	2002
Revenues	62	102	34	70	27	1,757	27	26
Operating Loss	(2,301)	(6,309)	(3,313)	(7,279)	(2,468)	(4,812)	(2,504)	(18,624)
Net Loss	(2,209)	(6,107)	(3,240)	(7,107)	(2,398)	(4,706)	(2,451)	(18,497)
Net Loss Per Share (Basic and Diluted)	(0.07)	(0.19)	(0.10)	(0.21)	(0.06)	(0.14)	(0.06)	(0.56)

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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).
3.4	Amendment for Reverse Split (previously filed as Exhibit 3.4 to Insmed Incorporated's Annual Report on Form 10-K for the year ended December 31, 2002 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).
4.6	Form of Stock and Warrant Purchase Agreement by and between Insmed Incorporated and each of the investors in the July 2003 private placement of common stock and warrants to purchase common stock (previously filed as Exhibit 4.6 to Insmed Incorporated's Registration Statement on Form S-3 (Registration No. 333-107308) on July 24, 2003 and incorporated herein by reference).
4.7	Form of Warrant issued by Insmed Incorporated to each of the investors in July 2003 private placement of common stock and warrants to purchase common stock (previously filed as Exhibit 4.7 to Insmed Incorporated's Registration Statement on Form S-3 (Registration No. 333-107308) on July 24, 2003 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).

Exhibit Number	Exhibit Title
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).
10.4+	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).
10.5+	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).
10.6+	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).
10.7	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).
10.8	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).
10.9	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).
10.10	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).
10.11+	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).
10.12	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).

Exhibit Number	Exhibit Title
10.13	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).
10.14	Termination Agreement, dated as of February 3, 2002, between Insmed Pharmaceuticals, Inc. and Taisho Pharmaceutical Co., Ltd (previously filed as Exhibit 10.14 to Insmed Incorporated's Annual Report of Form 10-K for the year ended December 31, 2002 and incorporated herein by reference).
10.15+	Agreement, dated as of July 25, 2002, between Insmed Incorporated and Avecia Limited (previously filed as Exhibit 10.15 to Insmed Incorporated's Annual Report of Form 10-K for the year ended December 31, 2002 and incorporated herein by reference).
10.16+	License and Supply Agreement, dated as of August 28, 2002, between Insmed Incorporated and Pharmacia AB (previously filed as Exhibit 10.16 to Insmed Incorporated's Annual Report of Form 10-K for the year ended December 31, 2002 and incorporated herein by reference).
10.17	Agreement, dated as of March 3, 2004, between Insmed Incorporated and Geoffrey Allan, Ph.D.
10.18*	License Agreement, dated as of January 19, 2004, between Insmed Incorporated and Fujisawa Pharmaceutical Co., Ltd.
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.
31.1	Certification of Geoffrey Allan, Ph.D., Chairman of the Board and Chief Executive Officer of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Kevin P. Tully C.G.A., Treasurer and Controller (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Geoffrey Allan, Ph.D., Chairman of the Board and Chief Executive Officer of Insmed Incorporated, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Kevin P. Tully, Treasurer and Controller (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

+ The Securities and Exchange Commission has granted confidential treatment with respect to certain information in these exhibits. The confidential portions of these exhibits have been omitted and filed separately with the Securities and Exchange Commission.

* Confidential treatment has been requested for certain portions of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

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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 22, 2004, with respect to the consolidated financial statements of Insmed Incorporated included in the Annual Report (Form 10-K) for the year ended December 31, 2003.

/s/ Ernst & Young LLP

McLean, Virginia
March 12, 2004

EXHIBIT 31.1

SECTION 302 CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER

I, Geoffrey Allan, Chairman of the Board and Chief Executive Officer of Insmed Incorporated, certify that:

(1) I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2003, of Insmed Incorporated;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) [Omitted in reliance on SEC Release No. 33-8238; 34-47986 Section III.E.]

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2004

/s/ Geoffrey Allan

Geoffrey Allan, Ph.D.
Chairman of the Board and Chief
Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

SECTION 302 CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER

I, Kevin P. Tully C.G.A., Treasurer and Controller of Insmed Incorporated, certify that:

(1) I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2003, of Insmed Incorporated;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) [Omitted in reliance on SEC Release No. 33-8238; 34-47986 Section III.E.]

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2004

/s/ Kevin P. Tully

Kevin P. Tully C.G.A.
Treasurer and Controller
(Principal Financial and Accounting Officer)

EXHIBIT 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Insmed Incorporated (the "Company") for the period ending December 31, 2003 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Geoffrey Allan, Ph.D., Chairman of the Board and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Geoffrey Allan, Ph.D.

Geoffrey Allan, Ph.D.
Chairman of the Board and
Chief Executive Officer
March 12, 2004

A signed original of this written statement required by § 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

EXHIBIT 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Insmed Incorporated (the "Company") for the period ending December 31, 2003 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Kevin P. Tully, Treasurer and Controller (Principal Financial and Accounting Officer) of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Kevin P. Tully

Kevin P. Tully C.G.A.
Treasurer and Controller
(Principal Financial and Accounting Officer)
March 12, 2004

A signed original of this written statement required by § 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Insmed Incorporated has filed an Annual Report on Form 10-K for 2003 with the Securities and Exchange Commission, which includes the complete financial statements of Insmed Incorporated. Copies of the Annual Report on Form 10-K can be obtained by contacting Insmed's Investor Relations department at bphillips@insmed.com or (804) 565-3041.

MANAGEMENT TEAM

Geoffrey Allan, Ph.D.
Chairman and Chief Executive Officer

Ronald D. Gunn, M.S., M.B.A.
Executive Vice President,
Chief Operating Officer

Andreas Sommer, Ph.D.
Chief Scientific Officer

Kevin P. Tully, CGA
Principal Financial Officer,
Treasurer, Controller

BOARD OF DIRECTORS

Kenneth G. Condon
Vice President for Financial Affairs
and Treasurer
Boston University

Graham K. Crooke, MB.BS.
Venture Capital Partner
Asset Management Company

Steinar J. Engelsen, M.D.
Director
Teknoinvest Management

Melvin Sharoky, M.D.
President
Somerset Pharmaceuticals

Randall W. Whitcomb, M.D.
Chief Medical Officer
QuatRx Pharmaceuticals

SHAREHOLDER INFORMATION

Corporate Address

Street Address
4851 Lake Brook Drive
Glen Allen, Virginia 23060

Mailing Address
P.O. Box 2400
Glen Allen, Virginia 23060

Contact Us
Telephone: (804) 565-3000
Fax: (804) 565-3500
Web: www.insmed.com

Stock Transfer Agent
Wachovia Bank, N.A.
1525 West W.T. Harris Blvd., 3 C 3
Charlotte, North Carolina 28288-1153

NASDAQ Symbol
The company's common stock is traded on the Nasdaq National Market under the symbol INSM.

Annual Meeting
The annual meeting of shareholders of Insmed Incorporated will be held at 9am EST on Wednesday, May 5, 2004, at the Hyatt Regency, Reston, Virginia.

INSMED
INCORPORATED

Insmed Incorporated
4851 Lake Brook Dr.
Glen Allen, VA 23060
www.insmed.com