INSMED INC
Form 10-K/A
June 10, 2005
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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K/A

AMENDMENT No. 4

(Mark One)

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

For the fiscal year ended December 31, 2004

OR

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

For the transition period from _____ to _____

Commission File Number 0-30739

INSMED INCORPORATED

(Exact name of registrant as specified in its charter)

Virginia **(State or other Jurisdiction of incorporation or organization)**	**54-1972729** **(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 [ü] 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 [ü] No [ ]

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant on June 30, 2004 was $86,024,160 (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, 2005, there were 44,986,996 shares of the registrant s common stock, $.01 par value, outstanding.

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Explanatory Note:

This Amendment No. 4 to the Annual Report on Form 10-K/A amends the Annual Report on Form 10-K of Insmed Incorporated (the Company) for the fiscal year ended December 31, 2004, filed with the Securities and Exchange Commission on March 16, 2005, as amended, solely to revise certain disclosure provided in the section entitled Management s Discussion and Analysis of Financial Condition and Results of Operations and in Note 1 to the Company s Consolidated Financial Statements. Except for the forgoing amended disclosures, the information in this Form 10-K/A has not been updated to reflect events that were not required to be disclosed in the filing which is being amended hereby.

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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 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.

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PART I

Insmed may from time to time make written or oral forward-looking statements , including statements contained in our filings with the Securities and Exchange Commission (including this Annual Report on Form 10-K and the Exhibits hereto and thereto), in our reports to stockholders and in other communications. Such statements give our current expectations or forecasts of future events; they do not relate strictly to historical or current facts. One can identify these forward-looking statements by their use of words such as may, could, should, would, believe, anticipate, estimate, expect, intend, plan, projects, outlook or similar expressions. In particular, these include statements relating to our beliefs, plans, objectives, goals, future actions, prospective products or product approvals, future performance or results of current and anticipated products, the outcome of contingencies, such as legal proceedings, and financial results. These statements are based upon the current beliefs and expectations of management and are subject to significant risks and uncertainties. Our actual results may differ materially from those set forth in the forward-looking statements. Forward-looking statements involve certain risks and uncertainties that are subject to change based on various factors (many of which are beyond our control). Factors that could cause or contribute to differences in our actual results include those discussed in Item 1 under the section entitled Risk Factors Related to Our Business, 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 on Form 10-K and in any other documents incorporated by reference. We undertake no obligation to publicly update forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in our 10-Q and 8-K reports to the Securities and Exchange Commission.

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. Currently, our development activities focus on drugs that modulate IGF-I activity in the human body. We currently have 3 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®) rhIGFBP-3 and INSM-18. 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

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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 Drug 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 over 100 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, severe insulin resistance, 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. A phase I clinical study to study safety and tolerance in human volunteers is in progress.

Insmed is also initiating clinical studies of a compound known as INSM-18, which has novel effects on the activity of the IGF-I and other receptors that can lead to the inhibition of growth of various tumors. Insmed is currently planning the clinical development of this compound in collaboration with the University of California, San Francisco School of Medicine and is preparing to initiate an exploratory clinical study in patients with relapsed prostate cancer.

Corporate History

In November 1999, Insmed Pharmaceuticals, Inc., our successor entity, entered into an agreement to acquire Celtrix Pharmaceuticals Inc. (Celtrix). Celtrix was a biopharmaceutical company focused on developing novel therapeutics for the treatment of seriously debilitating, degenerative conditions primarily associated with severe trauma, chronic diseases or aging. The transaction closed on May 31, 2000, at which time Celtrix and Insmed Pharmaceuticals, Inc. became wholly-owned subsidiaries of the newly formed entity, Insmed Incorporated, which was incorporated in the Commonwealth of Virgina on November 29, 1999.

On June 1, 2000, we began trading on The Nasdaq SmallCap Market on June 1, 2000 under the ticker symbol INSM. We moved from The Nasdaq SmallCap Market to the Nasdaq National Market on August 8, 2000.

Scientific Background

Role of IGF-I and IGFBP-3 in Growth

Insulin-like growth factor-I (IGF-I) is required for normal growth, development and metabolism. It is produced locally in tissues throughout the body, and also circulates in the blood to be delivered to target tissues. The majority of circulating IGF-I, which is largely produced by the liver, is bound to IGF binding proteins (IGFBPs), principally IGFBP-3. The major role of IGFBP-3 is to regulate the tissue distribution and activity of IGF-I.

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IGF-I binds to IGFBP-3 with high affinity to form a binary complex, which in turns binds to an acid-labile subunit (ALS) to form a ternary complex. All three components of the ternary complex are growth hormone (GH)-dependent. IGF-I is the principal mediator of the growth-promoting properties of GH. GH-induced IGF-I, that is either produced locally or delivered via the circulation, stimulates cartilage and bone and the growth plates of long bones and is necessary for normal accrual of peak bone mass.

Insufficient blood levels of IGF-I (IGF-I deficiency) during childhood and adolescence result in growth failure and short stature. In some cases, this is the result of inadequate GH quantity or bioactivity. Children with low levels of GH (GH deficiency) can generally be treated with recombinant human GH (rhGH) replacement therapy, resulting in normalization of IGF-I production and catch-up growth in most patients. However, there are a number of conditions in which IGF-I deficiency can occur despite normal or even elevated levels of GH. These abnormalities are known collectively as GH insensitivity syndrome (GHIS), and can result from either hereditary or acquired conditions. These forms of IGF-I deficiency are unresponsive to rhGH treatment.

IGF-I deficiency due to GHIS can be the result of genetic abnormalities involving the GH receptor or other genes in the GH signal transduction pathway or be the result of mutations in the IGF-I gene itself. Acquired conditions include the development of neutralizing antibodies to GH in response to rhGH treatment in children with deletions of the GH gene (GH deficiency type IA). Regardless of the cause of IGF-I deficiency, replacement therapy with rhIGF-I can correct the abnormality. Co-administration of rhIGF-I with rhIGFBP-3 can accomplish this in a more physiologic manner by delivering the IGF-I to tissues bound to its natural regulatory protein.

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

Insulin is the primary hormone responsible for controlling glucose metabolism. Although less potent than insulin, IGF-I is capable of stimulating hepatic and muscle glucose uptake. IGF-I can affect the set point for insulin action and, like insulin, block protein and lipid breakdown. IGF-I causes a decrease in circulating GH levels via negative feedback, which further affects glucose metabolism. Thus, the proper balance of insulin, GH and IGF-I is extremely important for normal glucose metabolism.

Short-term clinical studies with rhIGF-I/rhIGFBP-3 and longer-term studies with rhIGF-I reported in scientific literature demonstrate that IGF-I therapy can reduce insulin requirements, improve glycemic control, and increase insulin sensitivity in both type 1 and type 2 diabetes. Fujisawa Pharmaceutical Co., Ltd., with whom Insmed has 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, referred to as extreme insulin resistance. Extreme insulin resistance includes a number of chronic diseases distinguished by severe insensitivity to insulin due to inherited or acquired causes. Treatment with rhIGF-I/rhIGFBP-3 is intended to improved glycemic control and reduce insulin dose requirements in this patient population.

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. When bound to IGFBP-3, IGF-I is incapable of binding to the IGF-I receptor. IGFBP-3 also has independent actions of its own that can inhibit cell proliferation and stimulate cell death.

A number of epidemiological studies suggest that increased circulating levels of IGFBP-3 are associated with a decreased risk for the development of several common cancers, including those of the prostate, lung, rectum and bladder. Therefore, administration of rhIGFBP-3 may represent a novel therapeutic approach to a variety of human cancers. Insmed has initiated a clinical program with prominent oncologists 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, prostate and colon cancers.

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Insmed is also initiating clinical studies of a compound known as INSM-18, which has novel effects on the activity of the IGF-I and other receptors that can lead to the inhibition of growth of various tumors. Insmed is currently planning the clinical development of this compound in collaboration with the University of California, San Francisco School of Medicine and is preparing to initiate an exploratory clinical study in patients with relapsed prostate cancer.

Primary Therapeutic Indications

Growth Failure Due to GHIS Resulting in IGF-I Deficiency

GHIS is a condition affecting a specific subset of patients suffering from growth failure because of a deficiency in IGF-I. This deficiency can be due to hereditary or acquired defects in the GH receptor or GH signal transduction. Characteristics of this condition include:

- normal or elevated serum GH levels
- inability to generate normal IGF-I levels after GH provocation
- reduced serum IGF-I and IGFBP-3 levels
- severe postnatal growth failure and markedly reduced adult height (120-140 cm)
- truncal adiposity
- delayed skeletal maturation
- abnormal craniofacial development

Physicians use 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 the same age and sex. 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. Children with severe GHIS typically have height SDS < -3. Similarly, in evaluating IGF-I deficiency, physicians can use an IGF-I SDS < -2 to define abnormally low serum IGF-I levels.

Extreme Insulin Resistance

Insulin resistance describes an abnormality whereby the body is incapable of responding appropriately to circulating insulin. This abnormality can occur in many forms and results in varying degrees of disease severity. Extreme insulin resistance can result from defects in the insulin

receptor gene or other genes involved in insulin signal transduction. These conditions include:

Type A and Type B syndrome

Rabson-Mendenhall syndrome

Leprechaunism

Type A syndrome patients have high circulating concentrations of insulin with impaired glucose tolerance or diabetes. They also have hyperandrogenism, resulting in 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.

Type B syndrome is characterized by the presence of autoantibodies to the insulin receptor that interfere with proper receptor functioning. These patients have hyperinsulinism, erratic glycemic control, hyperandrogenism, and other autoimmune disorders. High doses of insulin fail to provide adequate glycemic control in these patients and there is no satisfactory treatment currently available.

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Rabson-Mendenhall syndrome and Leprechaunism are also characterized by high circulating concentrations of insulin with alternating episodes of hyperglycemia and hypoglycemia. They also have hyperandrogenism and growth failure. High doses of insulin fail to provide adequate glycemic control in these patients and there is no satisfactory treatment currently available.

Diabetes

Patients with type 1 diabetes are characterized by their inability to produce insulin. In these patients, insulin deficiency leads to glucose intolerance in childhood. In type 1 diabetes, down-regulation of GH receptors in the liver results in reduced circulating IGF-I levels, which can lead to GH hypersecretion. This in turn causes decreased insulin sensitivity and worsening of metabolic control. Treatment of type 1 diabetes with rhIGF-I/rhIGFBP-3 can reduce GH levels and improve insulin sensitivity and glycemic control, while decreasing insulin dose requirements.

Type 2 diabetes is characterized by insulin resistance. 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. Treatment of type 2 diabetics requiring insulin therapy with rhIGF-I/rhIGFBP-3 also leads to improved glycemic control while decreasing insulin dose requirement.

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. To this end, both IGFBP-3 and INSM-18 have emerged as promising novel treatments for a variety of cancer types. Both treatments interact with the IGF system to reduce tumor growth.

Business Strategy

Our focus is on the development and commercialization of products for the treatment of metabolic and endocrine diseases with unmet medical needs. Our initial goal is to obtain the approval of rhIGF-I/rhIGFBP-3 for the treatment of GHIS and establish proof-of-concept clinical data with rhIGFBP-3 in the treatment of breast or other cancers. 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 submitted a New Drug Application (NDA) on January 3, 2005 for the use of rhIGF-I/rhIGFBP-3 in the treatment of GHIS, which was accepted for review by the FDA on March 4, 2005. We are continuing our Phase III clinical trial in patients with GHIS in order to obtain long term data and plan to submit 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 similar circulating concentrations of IGF-I and efficacy results following administration of rhIGF-I/rhIGFBP-3 as was achieved in the Pharmacia studies following administration of rhIGF-I. Furthermore, these blood levels and efficacy 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 and clinical data suggest less severe side effects with rhIGF-I/rhIGFBP-3 when compared with rhIGF-I.

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Our strategy is to maintain a dual manufacturing source for our products. We currently manufacture rhIGF-I/rhIGFBP-3 at our manufacturing facility, Insmed Therapeutic Proteins (ITP), in Boulder, Colorado and plan to continue our manufacturing program with Avecia Limited, a third party contract manufacturer in the United Kingdom. Based on discussions with the FDA, we are conducting several studies, including analytical, pre-clinical and clinical to compare the drug substance previously manufactured at Avecia to the new drug substance produced at ITP. The results of this comparison will become part of our submissions 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 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 endocrinology centers where children with growth disorders are evaluated and treated. 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 partner with an established sales and marketing organization. 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 We are currently conducting a Phase I clinical study to establish the pharmacokinetic profile of rhIGFBP-3 and plan to 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.

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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 preclinical 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 $23.3 million in 2004, $7.1 million in 2003, and $18.1 million in 2002.

Strategic Relationships

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 obtained 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.

Tzamal Pharmaceutical

In October 2004, we entered into a letter of intent promotion agreement with Tzamal Pharma, a subsidiary of Fox Pharma headquartered in Jerusalem Israel. The agreement calls for Tzamal to be our exclusive distributor in Israel and Palestinian autonomous territories, West Bank and Gaza. The agreement has a term of one year and on the anniversary of the agreement it may be renewed via a joint agreement between Insmed and Tzamal for another twelve months.

Pharmacia Inc.

Pharmacia, Inc. was granted marketing approval in several European and Scandinavian countries for rhIGF-I in the treatment of GHIS. In August 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.

Avecia Limited

In July 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 the work performed under this agreement, we have paid process development and manufacturing costs associated with the production of rhIGF-I/rhIGFBP-3.

Patents and Proprietary Rights

Insmed Patent Portfolio

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 a foreign country. There also can be no assurance that a subsequent U.S. or foreign patent will later be held valid and enforceable.

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We hold 28 United States patents relating 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.

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.

In addition, foreign counterparts to the above-referenced U.S. patents have issued or are pending issue in the major pharmaceutical markets, such as Europe, Canada and Japan.

With respect to Europe, Insmed recently decided to withdraw one of its patents, EP 451,194 (the 194 patent), which is directed to compositions and methods of using IGFBP-3. This patent expires in 2009. We do not believe that a competitor is developing IGFBP-3 or will engage in activities encompassed by this patent prior to 2009. As such, the costs of maintaining this patent outweigh its estimated value. Therefore, Insmed has withdrawn its approval of the text of the 194 patent. As a result of this action, we expect the European Patent Office will soon revoke the 194 patent.

As part of our development and manufacturing agreement with Avecia Limited, we are currently negotiating to obtain 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.

Reflecting our commitment to safeguarding proprietary information, we require our employees and consultants to sign confidentiality agreements. These agreements prohibit unauthorized disclosure of Insmed s 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.

We note that 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 some cases, litigation or other proceedings may be necessary to enforce our patents or protect our know-how or other intellectual property rights. Any potential litigation could result in a substantial cost to us and a diversion of our resources. We cannot be sure that any of our patents will ultimately be held valid. An adverse outcome in any litigation or proceeding could subject us to significant liability.

Third-Party Patents

Third parties, including Genentech Inc. and Chiron Corporation 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.

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We can provide no assurance, however, that one of these third parties will not assert a contrary position in the future, for instance in the context of an infringement action. Likewise, we cannot predict with certainty the outcome of such a proceeding. We note, however, that an adverse ruling could impact our ability to make, use or sell our products. In any event, in some cases, litigation or other proceedings may be necessary to defend Insmed against claims of patent infringement.

In this regard, we note that on December 20, 2004, Tercica, Inc. and Genentech Inc. filed a complaint against Avecia Limited and Insmed, Inc. in the United Kingdom at the High Court of Justice, Chancery Division, Patents Court alleging infringement of EP patent No. 571,417 (the 417 patent). The 417 patent has claims directed to particular uses of a combination of IGFBP-3 and IGF-I. In the complaint, Tercica, Inc. asked the court for an injunction to restrain allegedly infringing activity, for a declaration that the 417 patent is valid and infringed, for an order requiring the delivery or destruction of allegedly infringing articles and materials and for an inquiry into possible economic damages.

On February 11, 2005, Avecia and Insmed filed a Defense and Counterclaim to Tercica Inc. s suit. In its Defense, Avecia and Insmed asserted, among other things, that the 417 patent is invalid and that the Claimant failed to properly register its license. In its Counterclaim, Avecia and Insmed also asked the court to revoke the 417 patent.

Insmed cannot predict with certainty the outcome of this proceeding. We note, however, that an adverse ruling could impact our ability to make, use or sell our products and would have a material adverse effect on our business, financial condition and results of operations.

In addition, Tercica, Inc. filed, on December 23, 2004, a complaint against Insmed in the United States District Court for the Northern District of California alleging infringement of U.S. patent Nos. 5,187,151 and 6,331,414. These patents are directed to certain methods of using IGF-I/IGFBP-3 and methods of producing human IGF-I, respectively. On February 16, 2005, Tercica, Inc. and Genentech, Inc. filed an Amended Complaint, adding allegations of infringement of U.S. patent No. 5,258,287 (the 287 patent). The claims of the 287 patent are directed to DNA encoding BP53 (i.e. IGFBP-3) and recombinant constructs, transformed host cells and methods for using same.

On February 18, 2005, Insmed filed a motion to dismiss the Amended Complaint. In the motion, Insmed asserted that all alleged activities fall within the statutory safe-harbor provided by 35 U.S.C. § 271(e)(1), commonly called the clinical trial exemption. This exemption prevents patent infringement actions from being filed against activities reasonably related to obtaining FDA approval of a product, such as when the product is still being tested in clinical trials. Insmed further asserted, among other things, that Plaintiffs have failed to state a claim for the requested relief, have not sued the proper party, have failed to name all the proper plaintiffs and have failed to establish the existence of a sufficiently real and substantial controversy between the parties. Insmed requested immediate dismissal or Summary Judgment against the plaintiff s allegation on these grounds.

Insmed cannot predict with certainty the outcome of this proceeding. We note, however, that an adverse ruling could impact our ability to make, use or sell our products and would have a material adverse effect on our business, financial condition and results of operations.

In addition, Novartis AG and Chiron Corporation have rights to United States and foreign patents relating to the use of IGF-1 for the treatment of type 1 diabetes, and Novartis owns United States and foreign patents relating to the treatment of osteoporosis with IGF-1. Genentech, Inc. owns U.S. and foreign patents directed to using IGF-1 to increase the growth rate of certain patients with non-GH-deficient short stature and patients having partial growth hormone insensitivity syndrome. We do not expect that we will infringe these patents. We can give no assurances, however, that such patents can be avoided, invalidated or licensed. Thus, the patents could potentially have an adverse effect on our ability to make, use or sell rhIGF-I/rhIGFBP-3 for certain indications.

Manufacturing

We currently rely on our wholly owned subsidiary, Insmed Therapeutic Proteins, as well as contract manufacturers to produce rhIGF-I/rhIGFBP-3 and rhIGFBP-3. If we are unable to establish our own capacity and

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maintain relationships with third parties for manufacturing sufficient quantities of our product candidates and their components which meet our planned time and cost parameters, the development and timing of our clinical trials and/or product commercialization may be adversely affected.

Our product candidates must be manufactured in a facility by processes that comply with current good manufacturing practices (cGMP) and other similar regulations. Prior to receiving marketing approval from the FDA, it is likely that the FDA will inspect our manufacturing facilities to ensure that our contract manufacturers and/or Insmed Therapeutic Proteins are in compliance with cGMP. If we are not in compliance with cGMP, the FDA may make us halt manufacturing until we can bring the facilities into compliance. This could take a substantial period of time and could adversely affect the development and timing of our clinical trials and/or product commercialization.

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 study requirements with rhIGF-I/rhIGFBP-3 previously produced by our subsidiary, Celtrix Pharmaceuticals Inc. or Avecia Limited, a contract manufacturer in Billingham, England.

In July 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 the work performed under this agreement, we have paid process development and manufacturing costs associated with the production of rhIGF-I/rhIGFBP-3.

We are currently manufacturing rhIGF-I/rhIGFBP-3 at Insmed Therapeutic Proteins in Boulder, Colorado. Celtrix Pharmaceuticals Inc. no longer produces rhIGF-I/rhIGFBP-3. We cannot guarantee that Insmed Therapeutic Proteins and 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

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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 United States and Europe is approved and marketed as replacement therapy for the treatment of GHIS. We are aware of only one other company, Tercica, Inc., that is pursuing development of a product for this indication. On February 28, 2005 Tercica announced that it had submitted a new drug application (NDA) for the use of rhIGF-I in the long term treatment of growth failure in children with a severe form of primary IGF deficiency. 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.

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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. The performance goals and procedures of the FDA Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER), as agreed to under the reauthorization of the prescription drug user fee program in the Food and Drug Administration Modernization Act of 1997, indicate the FDA is striving to review and act on 90% of standard NDA submissions filed during years 2003 through 2007 within 10 months of receipt and priority NDA submissions within 6 months of submission. 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.

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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 our 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 United States 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 United States 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 2003. 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, 2004, we had 55 full-time employees. Of these employees, 14 were engaged in research and development, 29 were engaged in manufacturing and 12 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.

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Risk Factors Related to Our Business

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, 2004, our accumulated deficit was $213.7 million. For the year ended December 31, 2004, our consolidated net loss was $27.2 million.

We currently have two lead product candidates, rhIGF-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 materially 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;

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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 approval 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 law suit 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

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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-I/rhIGFBP-3 in patients with GHIS and have included some data from this trial as pivotal information in a NDA submission to the FDA which was filed on January 3, 2005. We also plan to include the data from the trial in a MAA to the 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 materially 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 United States 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.

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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 have included data from this trial as a pivotal piece of information in a January 3, 2005 NDA submission to the FDA. We also plan to include the data 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 if 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 United States and European Union 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

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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 United States, and countries in the European Union 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 United States 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 United States 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 primary 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.

Failure to successfully manufacture our products could materially adversely affect our business, financial condition and results of operations. We intend to manufacture products at out ITP facility in Boulder, Colorado and enter into strategic alliances with other parties that have established commercial scale manufacturing capabilities. There can be no assurance that our ITP facility will have the capacity to produce the required products nor that we will enter into such strategic alliances on terms favorable to us or at all. If we are unable to increase production capacity at our ITP facility or 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.

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In addition, there can be no assurance that an adverse regulatory inspection at our ITP facility or at our contract manufacturers facilities would not impede our commercial supply capability. If we choose to commercialize such products solely on our own, it would be time consuming, resource intensive and capital intensive. If our contract manufacturers facilities or our facilities 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 at our ITP facility or in any of these third party 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 manufactured rhIGF-I/rhIGFBP-3 at our ITP facility and at Avecia s site at Billingham, England. At present, rhIGF-I/rhIGFBP-3 has never been manufactured by ITP or Avecia in quantities necessary for commercialization; we cannot guarantee that they will be able to produce the quantities of rhIGF-I/rhIGFBP-3 necessary for 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.

Our ITP facility and 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.

Product for our clinical trials is currently made at either our ITP facility or Avecia s manufacturing facility and then sent to an additional third party contract manufacture for sterile filtration and filling into vials. Should our ITP facility, Avecia s facility or our contract sterile filtration and filling manufacturer become unavailable to us for any reason, including damage from any event, including fire, flood, earthquake or terrorism, 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 if they are unwilling or unable to operate in compliance with cGMP or 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 and resources 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 ITP facility or our contract manufacturers fail to deliver sufficient 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.

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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 materially 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.

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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 materially 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 including the March 15, 2005 financing, 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

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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 materially 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 provide assurance 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 provide assurance 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

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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 materially 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 Inc. and Chiron Corporation 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 addition, Novartis AG and Chiron Corporation have rights to United States and foreign patents relating to the use of IGF-1 for the treatment of type 1 diabetes, and Novartis owns United States and foreign patents

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relating to the treatment of osteoporosis with IGF-1. Genentech, Inc. owns U.S. and foreign patents directed to using IGF-I to increase the growth rate of certain patients with non-GH-deficient short stature and patients having partial growth hormone insensitivity syndrome. We do not expect that we will infringe these patents. We can give no assurances, however, that such patents can be avoided, invalidated or licensed. Thus, the patents could potentially have an adverse effect on our ability to make, use or sell rhIGF-I/rhIGFBP-3 for certain indications.

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 can give no assurances 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.

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 materially 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 can give no assurances 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.

On December 20, 2004, Tercica, Inc. filed a complaint against Avecia Limited, Insmed, Inc. and Genentech, Inc. in the United Kingdom at the High Court of Justice, Chancery Division, Patents Court alleging infringement of EP patent No. 571,417 (the 417 patent). The 417 patent has claims directed to particular uses of a combination of IGFBP-3 and IGF-I. In the complaint, Tercica, Inc. asked the court for an injunction to restrain allegedly infringing activity, for a declaration that the 417 patent is valid and infringed, for an order requiring the delivery or destruction of allegedly infringing articles and materials and for an inquiry into possible economic damages.

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On February 11, 2005, Avecia and Insmed filed a Defense and Counterclaim to Tercica Inc. s suit. In its Defense, Avecia and Insmed asserted, among other things, that the 417 patent is invalid and that the Claimant failed to properly register its license. In this Counterclaim, Avecia and Insmed also asked the court to revoke the 417 patent.

Insmed cannot predict with certainty the outcome of this proceeding. We note, however, that an adverse ruling could impact our ability to make, use or sell our products.

Tercica, Inc. filed, on December 23, 2004, a complaint against Insmed in the United States District Court for the Northern District of California alleging infringement of U.S. patent Nos. 5,187,151 and 6,331,414. These patents are directed to certain methods of using IGF-I/IGFBP-3 and methods of producing human IGF-I, respectively. On February 16, 2005, Tercica, Inc. and Genentech, Inc. filed an Amended Complaint, adding allegations of infringement of U.S. patent No. 5,258,287 (the 287 patent). The claims of the 287 patent are directed to DNA encoding BP53 (i.e. IGFBP-3) and recombinant constructs, transformed host cells and methods for using same.

On February 18, 2005, Insmed filed a motion to dismiss the Amended Complaint. In the motion, Insmed asserted that all alleged activities fall within the statutory safe-harbor provided by 35 U.S.C. § 271(e)(1), commonly called the clinical trial exemption. This exemption prevents patent infringement actions from being filed against activities reasonably related to obtaining FDA approval of a product, such as when the product is still being tested in clinical trials. Insmed further asserted, among other things, that Plaintiffs have failed to state a claim for the requested relief, have not sued the proper party, have failed to name all the proper plaintiffs and have failed to establish the existence of a sufficiently real and substantial controversy between the parties. Insmed requested immediate dismissal or Summary Judgment against the plaintiff s allegation on these grounds.

Insmed cannot predict with certainty the outcome of this proceeding. We note, however, that an adverse ruling could impact our ability to make, use or sell our products.

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;

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ease of administration; and

marketing and sales capability.

Currently, no drug in the United States or Europe is approved and marketed as replacement therapy for the treatment of GHIS. We are aware of only one other company, Tercica, Inc., that is pursuing development of a product for this indication or a similar indication. On February 28, 2005 Tercica announced that it had submitted an NDA for the use of rhIGF-I in the long term treatment of growth failure in children with a severe form of primary IGF deficiency. 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.

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Our research, development and manufacturing 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, development and manufacturing 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 has been and 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

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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.

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.

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.

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.

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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 Securities and Exchange Commission. 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 Securities and Exchange Commission.

ITEM 2. PROPERTIES

We occupy 46,000 square feet of office and laboratory space in Glen Allen, Virginia and 30,000 square feet of manufacturing and warehouse space in Boulder, Colorado. Our annual cash cost for the Virginia space including utilities and services in 2004 was approximately $1.1 million under an operating lease that contains annual escalations of 1.75% and expires in October 2006. Our annual cash cost for the Colorado space including utilities and services in 2004 was approximately $0.6 million under an operating lease that contains an annual escalation of 3% and expires in February 2008. 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

On December 20, 2004, Tercica, Inc. and Genentech Inc. filed a complaint against Avecia Limited and Insmed, Inc. in the United Kingdom at the High Court of Justice, Chancery Division, Patents Court alleging infringement of EP patent No. 571,417 (the 417 patent). The 417 patent has claims directed to particular uses of a combination of IGFBP-3 and IGF-I. In the complaint, Tercica, Inc. asked the court for an injunction to restrain allegedly infringing activity, for a declaration that the 417 patent is valid and infringed, for an order requiring the delivery or destruction of allegedly infringing articles and materials and for an inquiry into possible economic damages.

On February 11, 2005, Avecia and Insmed filed a Defense and Counterclaim to Tercica Inc. s suit. In its Defense, Avecia and Insmed asserted, among other things, that the 417 patent is invalid and that the Claimant failed to properly register its license. In its Counterclaim, Avecia and Insmed also asked the court to revoke the 417 patent.

Insmed cannot predict with certainty the outcome of this proceeding. We note, however, that an adverse ruling could impact our ability to make, use or sell our products.

Tercica, Inc. filed, on December 23, 2004, a complaint against Insmed in the United States District Court for the Northern District of California alleging infringement of U.S. patent Nos. 5,187,151 and 6,331,414. These patents are directed to certain methods of using IGF-I/IGFBP-3 and methods of producing human IGF-I, respectively. On February 16, 2005, Tercica, Inc. and Genentech, Inc. filed an Amended Complaint, adding allegations of infringement of U.S. patent No. 5,258,287 (the 287 patent). The claims of the 287 patent are directed to DNA encoding BP53 (i.e. IGFBP-3) and recombinant constructs, transformed host cells and methods for using same.

On February 18, 2005, Insmed filed a motion to dismiss the Amended Complaint. In the motion, Insmed asserted that all alleged activities fall within the statutory safe-harbor provided by 35 U.S.C. § 271(e)(1), commonly called the clinical trial exemption. This exemption prevents patent infringement actions from being

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filed against activities reasonably related to obtaining FDA approval of a product, such as when the product is still being tested in clinical trials. Insmed further asserted, among other things, that Plaintiffs have failed to state a claim for the requested relief, have not sued the proper party, have failed to name all the proper plaintiffs and have failed to establish the existence of a sufficiently real and substantial controversy between the parties. Insmed requested immediate dismissal or Summary Judgment against the plaintiff s allegation on these grounds.

Insmed cannot predict with certainty the outcome of this proceeding. We note however, that an adverse ruling could impact our ability to make, use or sell our products.

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, 2004.

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PART II

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.

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 2004	**High**	**Low**
Fourth Quarter	$ 2.48	$ 1.24
Third Quarter	2.33	1.00
Second Quarter	3.40	1.98
First Quarter	4.28	2.87
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

On February 28, 2005, the last reported sale price for our common stock on the Nasdaq National Market was $1.29 per share. As of February 28, 2005, there were 565 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, 2004. 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, 2004 have been audited by

Ernst & Young LLP, our independent registered public accounting firm.

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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,					
	1999	2000	2001	2002	2003	2004
Historical Statement of Operations Data:						
Revenues	$	$ 60	$ 296	$ 1,955	$ 150	$ 137
Operating expenses:						
Research and development	5,657	21,608	35,506	18,077	7,140	23,320
General and administrative	2,189	5,989	4,881	2,984	3,477	4,242
Operational restructuring charge				2,533		
Goodwill write-off				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	27,562
Operating loss	(8,131)	(81,535)	(40,186)	(37,024)	(10,586)	(27,425)
Interest income, net	338	1,873	3,017	607	288	222
Loss before income taxes	(7,793)	(79,662)	(37,169)	(36,417)	(10,298)	(27,203)
Income tax expense		200				
Net loss	(7,793)	(79,862)	(37,169)	(36,417)	(10,298)	(27,203)
Basic and diluted net loss per share	(2.47)	(4.36)	(1.13)	(1.10)	(0.29)	(0.69)
Weighted average shares	3,155	18,319	32,871	33,066	35,600	39,160
Historical Balance Sheet Data:						
Cash, cash equivalents and marketable securities	$ 4,635	$ 83,083	$ 51,250	$ 27,337	$ 29,526	$ 9,222
Total assets	5,296	102,718	71,606	28,308	29,812	13,011
Stockholders equity	4,462	96,782	59,695	23,446	26,220	7,235

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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 3 lead drug candidates rhIGF-I/rhIGFBP-3, rhIGFBP-3 and INSM-18. During 2004 we initiated a pivotal Phase III study with rhIGF-I/rhIGFBP-3 in GHIS and a Phase I study with rhIGFBP-3 in cancer. Also during 2004 we were successful in manufacturing clinical grade rhIGF-I/rhIGFBP-3 at Avecia and commissioned our ITP facility in Boulder, Colorado. On January 3, 2005 we submitted an NDA to the FDA for the use of rhIGF-1/rhIGFBP-3 in the treatment of GHIS, and on March 4, 2005 we received acceptance of the filing for FDA review. We are continuing our Phase III clinical trial in order to obtain long term data and plan to submit a MAA to the EMEA for this indication. Our plans for 2005 include:

Obtain NDA approval for rhIGF-I/rhIGFBP-3 in GHIS

Initiate clinical trials to expand rhIGF-I/rhIGFBP-3 into additional niche indications

Establish commercial activities consistent with FDA approval process

Capitalize through debt/equity and partnership fees to sustain 2005/2006 operations

Establish European partner for rhIGF-I/rhIGFBP-3 and global partner for rhIGFBP-3

Aggressively defend patent lawsuits in the United States and United Kingdom

We have not been profitable and have accumulated deficits of approximately $213.7 million through December 31, 2004. 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.

Research and Development Activities

We are engaged in the research and development of proposed drug products for the treatment of metabolic diseases and endocrine disorders. All of our research and development expenditures, whether conducted by our own staff or by external scientists on our behalf and at our expense, are recorded as expenses as incurred and amounted to approximately $106 million dollars for the period since inception, in November 1999, through December 31, 2004, and $18 million, $7 million and $23 million in the years ended December 31, 2002, 2003 and 2004. Research and development expenses consist primarily of salaries and related expenses, costs to develop and manufacture products and amounts paid to

contract research organizations, hospitals and laboratories for the provision of services and materials for drug development and clinical trials.

Our leading drug candidate, rhIGF-I/rhIGFBP-3, or SomatoKine®, is currently in Phase III clinical trials for the treatment of GHIS. We have filed an NDA for this drug in the GHIS indication, which was accepted for review by the FDA. We have also received priority review for SomatoKine® and the FDA has notified us that the User Fee Goal Date is July 3, 2005, however there can be no assurance that the FDA will act by this date. SomatoKine® has also been granted orphan drug designation for the GHIS indication and other indications. Substantially all of our research and development expenditures for fiscal 2003 and 2004 have been related to SomatoKine®.

Our research and development efforts for other products are in their early stages and include primarily research and development regarding rhIGFBP-3 for the treatment of various cancers and INSM-18 for the treatment of various tumors. These products are either in pre-clinical stages or, Phase I and II clinical trials. All

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of our research and development expenditures related to these early-stage products and our efforts associated with SomatoKine® are significantly interrelated as they are all associated with drugs that modulate IGF-I activity in the human body. A significant finding in any one drug for a particular indication may provide benefits to our efforts across all of these products. All of these products also share a substantial amount of our common fixed costs such as salaries, facility costs, utilities and maintenance. Given the small portion of research and development expenses that are related to products other than SomatoKine® we have determined that very limited benefits would be obtained from implementing cost tracking systems that would be necessary to allow for cost information on a product-by-product basis.

In the near term, Insmed intends to focus substantially all of its research and development resources on the completion of phase III clinical trials for SomatoKine® in the GHIS indication and expansion of SomatoKine® into other indications. Our efforts to obtain FDA approval for SomatoKine® for the GHIS indication will be our main focus for the remainder of fiscal 2005. We estimate that our research and development expenditures to complete development of SomatoKine in this indication will be in the range of between $20 million to $23 million for the current fiscal year. Our plans to expand SomatoKine® into additional indications are expected to represent our main research and development focus beginning in 2006. Our thrust to develop our other early-stage products will continue but we expect those efforts to account for a much smaller portion of Insmed s research and development expenditures. These estimates are based on currently available information and, due to a number of factors, no assurance can be provided that this project will not take longer to complete or cost more than we have currently estimated. The full cost and completion dates, through commercialization, of these research and development efforts, are dependent on the results of our Phase III clinical trial, together with the review of our NDA by the FDA.

Our clinical trials with respect to SomatoKine® are subject to numerous risks and uncertainties that are outside of our control, including the possibility that necessary regulatory approvals may not be obtained. For example, the duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during the clinical trial protocol, including, among others, the following:

- the number of patients that ultimately participate in the trial;
- the duration of patient follow-up that is determined to be appropriate in view of results;
- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patient subjects; and
- the efficacy and safety profile of the product candidate.

Our clinical trials may also be subject to delays or rejections based on our inability to enroll patients at the rate that we expect or our inability to produce clinical trial material in sufficient quantities and of sufficient quality to meet the schedule for our planned clinical trials.

Moreover, all of our product candidates and particularly those that are in the pre-clinical or early clinical trial stage must overcome significant regulatory, technological, manufacturing and marketing challenges before they can be successfully commercialized. Some of these projects may never reach the clinical trial stage of research and development. As pre-clinical studies and clinical trials progress, we may determine that collaborative relationships will be necessary to help us further develop or to commercialize our product candidates, but such relationships may be difficult or impossible to arrange. Our projects or intended projects may also be subject to change from time to time as we evaluate our research and development priorities and available resources.

Any significant delays that occur or additional expenses that we incur may have a material adverse affect on our financial position and require us to raise additional capital sooner or in larger amounts than is presently expected. In addition, as a result of the risks and uncertainties related to the development and approval of our drug candidates and the additional uncertainties related to our ability to market and sell these products once approved for commercial sale, we are unable to provide a meaningful prediction regarding the period in which material net cash inflows from any of these projects are expected to become available.

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Results of Operations

Year Ended December 31, 2004 compared to Year Ended December 31, 2003

For the year ended December 31, 2004, we recorded a net loss of $27.2 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) increased $16.2 million from $7.1 million in 2003 to $23.3 million in 2004. This rise in spending resulted from a broader clinical trials program and an increase in manufacturing activity at our ITP facility and at our contract manufacturer Avecia to produce rhIGF-I/rhIGFBP-3 for our clinical trials,

General and administrative expenses increased $0.7 million from $3.6 million for 2003 to $4.3 million for 2004. The increase was due to higher external service and personnel costs in support of our business. Revenues decreased $13,000 from $150,000 in 2003 to $137,000 in 2004 due to a slight decline in royalties.

As of December 31, 2004, cash and cash equivalents decreased to $9.2 million from $29.5 million at December 31, 2003. As a result of a lower average cash balance and lower interest rates in 2004 compared to 2003, net interest income decreased $66,000 from $288,000 in 2003 to $222,000 million in 2004.

Accounts payable and accrued project costs increased $1.1 million from $2.4 million at December 31, 2003 to $3.5 million at December 31, 2004 as a result of increased clinical and manufacturing activity. Stockholders equity decreased $19.0 million mainly as a result of the net loss for 2004 of $27.2 million being partially offset by approximately $8.0 million in net proceeds received in connection with a private placement of our common stock on November 8, 2004. The accumulated deficit at December 31, 2004 increased to approximately $213.8 million due to our 2004 net loss of $27.2 million.

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, was 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

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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 2003 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 2004. The accumulated deficit at December 31, 2003 increased to approximately $186.5 million due to our 2003 net loss of $10.3 million.

Liquidity and Capital Resources

There is considerable time and cost associated with developing a potential drug or pharmaceutical product to the point where FDA approval for sales is received. In our financial management, we seek to raise the funds necessary for such development primarily through the issuance of equity securities in private placement transactions. However, it is our intention to pursue additional financing options, including entering into agreements with corporate partners in order to provide milestone payments, license fees and equity investments.

Capital Requirements

Expenditures in the year ended December 31, 2004 were principally related to the research and development, increased clinical trial activity and manufacturing activities at our site in Boulder, Colorado, as well as administrative support activities. In the short-term, we will need to raise substantial additional funds to continue the development and approval process with respect to our lead drug products. In the longer-term, we will require substantial additional funds for the commercialization of those products. Our continuation as a going concern depends on our ability to obtain such additional financing and, ultimately, to generate positive cash flow and attain profitability. 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.

Planned expenditures in 2005 include the funding of our ongoing R & D activity, such as manufacturing and clinical trial costs, General and Administrative support costs plus initial commercialization efforts associated with the anticipated approval of our NDA.

Capital Resources

We have funded our operations to date primarily through public and private placements of equity securities. We plan to continue incurring losses as we expand our research and development and do not expect material revenues for at least the next several years. At December 31, 2004, our

cash and cash investments were approximately $9.2 million and were invested in money market instruments. This is a decrease from $29.5 million at December 31, 2003, despite the conclusion, in November 2004, of a private placement of 6,455,551 shares of our common stock to a group of institutional investors at a price of $1.35 per share, which raised a total of approximately $8.7 million. The placement agent in the transaction received approximately $572,000 in fees and expenses (including fees paid to the placement agent s attorneys) resulting in net proceeds of approximately $8.0 million. We also issued warrants to purchase an additional 3,227,775 shares of our common stock with an exercise price of $2.00 per share.

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On March 15, 2005, we entered into several purchase agreements with a group of institutional investors, pursuant to which we issued and sold to the investors approximately $35,000,000 aggregate principal amount of 5.5% convertible notes, which notes are convertible into our common stock, par value $0.01 per share, as well as warrants to purchase, in the aggregate, 14,864,883 shares of our common stock, at an exercise price of $1.36 per share. The principal of each note will mature and be payable in nine quarterly installments of approximately $3,890,000 commencing on March 1, 2008. Any outstanding notes must be repaid in cash or converted by March 1, 2010. Commencing on June 1, 2005, the notes will bear interest at a rate of 5.5% per annum and is payable quarterly commencing on March 1, 2008. The holders of the notes may convert the notes into our common stock at a conversion price of $1.295 per share as adjusted in accordance with certain adjustments for stock splits, dividends and the like at any time prior to the close of business on March 1, 2010. The notes are convertible into, in the aggregate, 27,027,027 shares of our common stock. The warrants are immediately exercisable for 14,864,883 shares of our common stock at an exercise price of $1.36 per share. The warrants will expire on March 15, 2010. The holders of the notes have the right to require us to repurchase the notes with cash payments up on the occurrence of specified events of default and repurchase events. The investors also have the right to participate in future financings undertaken by us prior to March 16, 2005, subject to certain exceptions. In connection with issuance of the notes and warrants, we entered into registration rights agreements with the investors pursuant to which we agreed to file a Registration Statement under the Securities Act of 1933, registering for resale the shares of common stock issuable upon the conversion of the notes or exercise of the warrants.

With this additional funding the company believes it has sufficient capital resources to fund our operations through the next twelve months.

Our business strategy contemplates raising additional capital through equity sales. We also plan to enter into agreements with corporate partners in order to fund research and development and to provide milestone payments, license fees and equity investments to fund our 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**	**1-4 years**
Operating Lease Obligations	2,472	1,153	1,319
Total	$ 2,472	$ 1,153	$ 1,319

Critical Accounting Policies

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. 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

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other conditions had prevailed. For additional accounting policies, see Note 1 to our consolidated financial statements Description of the Business and Summary of Significant Accounting Policies

Research and Development

Research and development costs are expensed as incurred. Research and development expenses consist primarily of salaries and related expenses, cost to develop and manufacture products and amounts paid to contract research organizations, hospitals and laboratories for the provision of services and materials for drug development and clinical trials. We do not have separate accounting policies for internal or external research and development and we do not conduct any research and development for others. Our expenses related to clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with third party organizations that conduct and manage clinical trials on our behalf. These contracts set forth the scope of work to be completed at a fixed fee or amount per patient enrolled. Payments under these contracts depend on performance criteria such as the successful enrollment of patients or the completion of clinical trial milestones. Expenses are accrued based on contracted amounts applied to the level of patient enrollment and to activity according to the clinical trial protocol.

Our expenses relating to contract manufacturing of clinical material are based on agreements reached with the contract manufacturer. The contract identifies the amount of clinical material to be manufactured, the time for manufacture, and other development work to be completed in supporting the manufacturing of the clinical material. In general, the contract and the work to be completed are in phases, and we accrue expenses for these contracts based upon the initiation and timing of each phase.

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 2. 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, 2004, had $9.2 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, 2004, 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 2005, 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.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Based on their evaluation, as of December 31, 2004, Insmed Incorporated s Chief Executive Officer and Chief Financial Officer have concluded that Insmed Incorporated s disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) are effective.

Management s Report on Internal Control Over Financial Reporting

The management of Insmed Incorporated is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended). Insmed Incorporated s internal control over financial reporting was designed to provide reasonable assurance to Insmed Incorporated s management and board of directors regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Insmed Incorporated s management assessed the effectiveness of Insmed Incorporated s internal control over financial reporting as of December 31, 2004 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control Integrated Framework*. Management s assessment included an evaluation of the design of Insmed Incorporated s internal control over financial reporting and testing of the operational effectiveness of Insmed Incorporated s internal control over financial reporting. Based on this assessment, Insmed Incorporated s management concluded that, as of December 31, 2004, Insmed Incorporated s internal control over financial reporting was effective.

Ernst & Young LLP, an independent registered public accounting firm, has issued an audit report on management s assessment of Insmed Incorporated s internal control over financial reporting. The report of Ernst & Young LLP is contained in Item 8 of this Annual Report on Form 10-K.

There have been no changes in Insmed Incorporated s internal control over financial reporting that occurred during the three months ended December 31, 2004 that have materially affected, or are reasonably likely to materially affect, such internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The Board of Directors

Our Articles of Incorporation, as amended, provide that our Board shall consist of not more than 12 directors, with the exact number to be prescribed by our Bylaws. Our Bylaws provide that the number of directors constituting our Board shall be designated by a resolution of the Board but shall be not less than six nor more than 10. Our Board has adopted a resolution designating six directors. The directors are divided into three classes Class I, Class II and Class III as nearly equal in number as possible. Each class of directors serves for three years on a staggered term basis.

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The Board has determined that the following members of the Board are independent, as that term is defined under the general independence standards in the listing standards of The Nasdaq Stock Market, Inc., and our Corporate Governance Guidelines: Mr. Kenneth G. Condon, C.P.A., C.F.P., M.B.A., Dr. Steinar J. Engelsen, Dr. Melvin Sharoky, Dr. Graham K. Crooke and Dr. Randall W. Whitcomb. The Board has adopted, as part of our Corporate Governance Guidelines, categorical standards to assist it in making these independence determinations. Our Corporate Governance Guidelines are available on our website at *www.insmed.com*.

The Board has nominated one Class II director, Dr. Crooke, for election at the 2005 Annual Meeting of Shareholders for the term expiring at the 2008 Annual Meeting. The term of the Class III directors, Drs. Allan, Sharoky and Whitcomb, will expire at the 2006 Annual Meeting of Shareholders. The term of the Class I directors, Mr. Condon and Dr. Engelsen, will expire at the 2007 Annual Meeting of Shareholders.

The following table sets forth the nominee to be elected at the 2005 Annual Meeting of Shareholders and continuing directors and, for each director whose term of office will extend beyond the meeting, the year such nominee or director was first elected a director, the positions currently held by the nominee and each director with the Company, the year each nominee s or director s current term will expire and the current class of director of the nominee and each director:

Nominee s or Director s Name	Age	Position(s) with the Company	Year First Became Director and Year Current Term Will Expire	Class of Director
Nominee for Class II Director:				
Graham K. Crooke, MB.BS	46	Director	1999-2005	II
Continuing Directors:				
Geoffrey Allan, Ph.D. (1)	51	President, Chief Executive Officer, Chairman of the Board, Director	1999-2006	III
Melvin Sharoky, M.D. (2)(3)(4)	54	Director	2001-2006	III
Randall W. Whitcomb, M.D. (4)	50	Director	2001-2006	III
Kenneth G. Condon, C.P.A., C.F.P., M.B.A. (2)(3)	57	Director	1999-2007	I
Steinar J. Engelsen, M.D. (2)(3)	54	Director	1999-2007	I

(1) Chairman of the Board
(2) Member of Audit Committee
(3) Member of Compensation Committee
(4) Member of Nominations and Governance Committee

Business Experience

Graham K. Crooke, MB.BS age 46. Dr. Crooke has been a director of Insmed since our inception in November 1999 and of Insmed Pharmaceuticals since 1996. In April 2000, Dr. Crooke became a partner of Asset Management Company, a venture capital firm focusing on investments in early stage information technology and life sciences companies. Previously, from September 1997 through March 2000, Dr. Crooke was a partner at Ticonderoga Capital, a venture capital firm, where he focused on biotechnology and healthcare service investments. From April 1992 until September 1997, Dr. Crooke was a vice president of Dillon Read Venture Capital, a venture capital firm and predecessor to Ticonderoga. Prior to that, Dr. Crooke worked with the healthcare practice of Booz, Allen & Hamilton, Inc., a management consulting firm, was a product manager at Molecular Devices Corporation, a developer of bioanalytical measurement systems, and, from 1984 to 1986, practiced

medicine at major teaching hospitals in Western Australia. He received his medical degree from the University of Western Australia and an M.B.A. from the Stanford Graduate School of Business.

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Geoffrey Allan, Ph.D. age 51. Dr. Allan has served as our President, Chief Executive Officer and Chairman of the Board since our inception in November 1999. Dr. Allan has been President and a director of Insmed Pharmaceuticals Inc., our predecessor, since January 1994 and has 24 years of experience in pharmaceutical drug development. Prior to joining Insmed Pharmaceuticals, Dr. Allan served as Vice President, Drug Development at Whitby Research, Inc., a pharmaceutical company. Before his association with Whitby Research, Dr. Allan was the Head of the Cardiovascular Section at Wellcome Research Laboratories. Dr. Allan received his Ph.D. in Pharmacology from Cornell University Medical College.

Melvin Sharoky, M. D. age 54. Dr. Sharoky has been a director of Insmed since his election on May 16, 2001. Since January 1, 2002, he has been President and CEO of Somerset Pharmaceuticals, Inc., a research and development pharmaceutical company which markets Eldepryl® for the treatment of patients with late stage Parkinson s disease having previously served as President of Somerset Pharmaceuticals from July 1995 to June 30, 2001. From June 30, 2001 to January 1, 2002, Dr. Sharoky was retired. From July 1995 through January 1998, Dr. Sharoky was President of Watson Pharmaceuticals, Inc., a leading specialty pharmaceutical company, and from February 1993 to January 1998 he was also President and Chief Executive Officer of its wholly-owned subsidiary, Circa Pharmaceuticals, Inc., which develops, manufactures and markets solid dosage generic pharmaceutical products to wholesale distributors. Dr. Sharoky joined Circa Pharmaceuticals in July 1988 as Medical Director, served as Senior Vice President and Director of Research and Development from April 1991 to August 1992, and as Executive Vice President and Director of Research and Development from August 1992 to January 1993. Prior to this, from February 1986 to June 1988 he was Vice President and Chief Medical Officer of Pharmakinetics Laboratories, Inc. Dr. Sharoky serves on the board of directors of Andrx Corporation, a specialty pharmaceutical company. Dr. Sharoky received a B.A. in biology from the University of Maryland in Baltimore County and an M.D. from the University of Maryland School of Medicine.

Randall W. Whitcomb, M. D. age 50. Dr. Whitcomb has been a director of Insmed since November 15, 2001. Since 2001, Dr. Whitcomb has been Chief Medical Officer at Quatrx Pharmaceuticals, Inc., a privately-held, drug development company focusing on proteins in the cell nucleus that act as receivers for key hormones that regulate certain metabolic and developmental processes in the body. From 1992 through 2000, he held various management positions with Parke-Davis Pharmaceutical Research, Inc., a division of Warner Lambert Company, finally serving as Vice President of Drug Development with particular responsibility for the development and approval of products for women s health care and diabetes. After the merger of Warner Lambert into Pfizer, Inc., Dr. Whitcomb was Vice-President Global Project Management for Pfizer Global Research and Development. From 1987 through 1992 he was on the faculty of Massachusetts General Hospital and Harvard Medical School. He received his B.A. degree from Tabor College and his M.D. degree from the University of Kansas.

Kenneth G. Condon C.P.A., C.F.P., M.B.A. age 57. Mr. Condon has been a director of Insmed since our inception in November 1999 and of Insmed Pharmaceuticals since 1997. Mr. Condon serves as Chief Financial Officer of Boston University, a position he has held from 1975 to present. He is also a Trustee of Newbury College. He was formerly Chairman of the Board of BayFunds, a $1.8 billion mutual fund family; a former director of BayBank Harvard Trust; a former member of the BankBoston Advisory Board; a former director of the BayBank Trust Board; a former director of Seragen, Inc., a biotechnology firm; a former director, Chapter Secretary, Treasurer and President of the Financial Executives Institute of Massachusetts; and Director, Treasurer of the Boston Municipal Research Bureau. Before 1975, Mr. Condon was a Senior Accountant with the CPA firm of Arthur Andersen & Co. in Boston. He received his B.A. degree in Economics and Mathematics from Tufts University, and an M.B.A. in Finance from the Wharton School of Finance, University of Pennsylvania. Mr. Condon is both a Certified Public Accountant and a Certified Financial Planner.

Steinar J. Engelsen, M.D. age 54. Dr. Engelsen has been a director of Insmed since our inception in November 1999 and of Insmed Pharmaceuticals since 1998. Since November 1996, Dr. Engelsen has been a partner of Teknoinvest Management AS, a venture capital firm based in Norway. From 1989 until October 1996, Dr. Engelsen held various management positions within Hafslund Nycomed AS, a pharmaceutical company

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based in Europe, and affiliated companies. He was responsible for therapeutic research and development, most recently serving as Senior Vice President, Research and Development of Nycomed Pharma AS from January 1994 until October 1996. In addition, from January to November 2000, Dr. Engelsen was acting chief executive officer of Centaur Pharmaceuticals, Inc., a biopharmaceutical company. Dr. Engelsen also served as chairman of the board of directors of Centaur. Dr. Engelsen received a M.Sc. in nuclear chemistry and an M.D. from the University of Oslo, and is a Certified European Financial Analyst.

Executive Officers

The following table sets forth the executive officers of the Company, their ages, and the positions currently held by each such person with the Company immediately prior to the meeting:

Name	Age	Position	Term of Office
Geoffrey Allan, Ph.D.	51	President, Chief Executive Officer, Chairman of the Board, and Director	Nov. 1999
Ronald D. Gunn, M.B.A., M.S.	44	Executive Vice President and Chief Operating Officer	Feb. 2004
Andreas Sommer, Ph.D.	63	Chief Scientific Officer	March 2004
Kevin P. Tully, C.G.A.	51	Principal Financial Officer, Treasurer and Controller	Jan. 2002
Philip J. Young	47	Chief Business Officer and Executive Vice President, Commercial Operations	April 2004

Business Experience

Ronald D. Gunn, M.B.A., M.S. age 44. In February 2004, Mr. Gunn was appointed Executive Vice President and Chief Operating Officer. From June 2003 until his appointment as Executive Vice President and Chief Operating Officer, Mr. Gunn served as Executive Vice President. Since our inception in November 1999 until his election as Executive Vice President, Mr. Gunn served as our Vice President, Business Development. From January 1999 to November 1999, Mr. Gunn served as Vice President, Business Development and previously as Director of Business Development and of Clinical Operations at Insmed Pharmaceuticals. Mr. Gunn joined our predecessor in 1996 and has more than 18 years of experience in pharmaceutical drug development. Prior to joining Insmed, Mr. Gunn served as Clinical Affairs Officer with Finnish bioscience company, Leiras, Inc. Mr. Gunn received his M.S. and M.B.A. from Virginia Commonwealth University.

Andreas Sommer, Ph.D. age 63. In March 2004, Dr. Sommer became our Chief Scientific Officer. Dr. Sommer joined Insmed in August 2000 as Principal Scientist following Insmed s acquisition of Celtrix Pharmaceuticals, Inc. (Celtrix). From April 1995 to May 2000, Dr. Sommer served as Chief Executive Officer and President of Celtrix and served as a director of Celtrix from May 1994 to May 2000. Previously, Dr. Sommer served as Senior Vice President and as Vice President, Research of Celtrix following Celtrix s merger with BioGrowth, Inc. From 1989 to 1991, Dr. Sommer served as Vice President, Research and Development of BioGrowth. He received his Ph.D. in microbiology from the University of California.

Kevin P. Tully, C.G.A. age 51. In January 2002, Mr. Tully became our Treasurer, Controller and Principal Financial Officer. From August 2001 until his election as Treasurer, he served as Senior Director, Finance and Administration. Mr. Tully joined Insmed in March 2001 as Director of Finance and has over 30 years of experience across Europe and the Americas covering finance, marketing and manufacturing. Prior to joining

Insmed, Mr. Tully served as Vice President of Finance Europe, and Vice President, Finance and Administration Americas for Albright and Wilson Ltd., an international chemical producer. Mr. Tully received his O.N.C. in Business and Administration from St. Helens College in England and is a Certified General Accountant.

Philip J. Young age 47. In April 2004, Mr. Young was appointed Chief Business Officer and Executive Vice President of Commercial Operations of Insmed Incorporated. Prior to joining Insmed, Mr. Young served as

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President and Chief Operations Officer for AGY Therapeutics and Chief Executive Officer of GanTech International. From 1998-2000, Mr. Young was Vice President and General Manager of Neurex Pharmaceuticals, where he was responsible for developing and managing the commercial and clinical strategies for new product launches and expanding label indications. Prior to Neurex, Mr. Young was Business Director and General Manager of the Peptide Hormones Division at Pharmacia (Pfizer) where under his leadership strategies were developed which led to the successful launch of Genotropin for pediatric and adult growth hormone deficiency. Mr. Young also served for seven years at Genentech where he was the Product Manager of Growth Hormone Products.

Audit Committee

Our Audit Committee currently consists of Mr. Condon (Chairman), and Drs. Engelsen and Sharoky. During 2004, the Audit Committee held six meetings. Mr. Condon and Dr. Sharoky attended all of the meetings and Dr. Engelsen attended five of the meetings. The Audit Committee (i) recommends the selection of independent accountants and auditors, (ii) reviews the scope of the accountants audit and approves any non-audit services to be performed by the independent accountants and (iii) reviews annual audits and accounting practices. The Board has adopted a written charter for the Audit Committee, which is available on our website at *www.insmed.com*.

Insmed Common Stock is listed on the Nasdaq National Market and, as such, we are governed by the listing standards of the National Association of Securities Dealers, Inc. (the NASD). Rule 4350(d)(2)(A) of the NASD s listing standards requires that our Audit Committee be comprised of at least three members, each of whom must be an independent director as defined in Rule 4200(a)(15) of the listing standards of the NASD. The Board has determined that all three of our Audit Committee members, Mr. Condon and Drs. Engelsen and Sharoky, are independent directors as defined by the listing standards of the NASD.

The Board has determined that Mr. Condon is an audit committee financial expert as that term is defined in the rules promulgated by the Securities and Exchange Commission pursuant to the Sarbanes-Oxley Act of 2002.

The Board has determined that each of the members of the Audit Committee is able to read and understand fundamental financial statements, including our balance sheet, consolidated statement of operations and consolidated statement of cash flows, and has accounting or related financial management expertise, as such terms are interpreted by the Board.

The Audit Committee s pre-approval policies and procedures are detailed in Item 14 of this Annual Report on Form 10-K.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires that our directors, officers and persons who own more than 10% of a registered class of our equity securities file reports of ownership and changes in ownership of such securities with the Securities and Exchange Commission and The Nasdaq Stock Market, Inc. Directors, officers and beneficial owners of more than 10% of Insmed Common Stock are required by applicable regulations to furnish us with copies of all Section 16(a) forms they file. Based solely upon a review of the copies of the forms and information furnished to us, we believe that during the fiscal year ended December 31, 2004 all filing requirements applicable to our directors, officers and beneficial owners of more than 10% of Insmed Common Stock were satisfied, except that Statements of Changes in Beneficial Ownership of Securities on Form 4 for each of Drs. Crooke, Engelsen, Sharoky and Whitcomb and Mr. Condon to report the stock option grants on May 5, 2004 of 17,500 shares were filed late. In addition, it has come to our attention that Statements of Changes in Beneficial Ownership on Form 4 for each of Drs.

Crooke, Engelsen, Sharoky and Whitcomb and Mr. Condon to report stock option grants on May 12, 2003 were also filed late.

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Code of Ethics

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 Securities and Exchange Commission.

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ITEM 11. EXECUTIVE COMPENSATION

Executive Officer Compensation

Summary Compensation Table. The following table sets forth information for the fiscal years ended December 31, 2004, 2003 and 2002, respectively, with respect to certain compensation paid by us to our named executive officers, as such term is defined in Item 402(a)(3) of Regulation S-K. Other than the executive officers listed below, none of our current executive officers received total cash compensation from us in excess of $100,000 for any of the fiscal years ended December 31, 2004, 2003 and 2002.

		Annual Compensation ($)(1)				Long Term Compensation (1)		
Name and Principal Position	Fiscal Year	Salary (2)	Bonus (3)	Other Annual Compensation (4)	Restricted Stock Awards ($)	Securities Underlying Options/ SARs(#)	Long Term Incentive Plan Payout ($)	All Other Compensation ($)(5)
Geoffrey Allan, Ph.D.	2004	395,200	98,800	21,717				2,075
	2003	395,200	197,600	18,941		150,000		2,075
Chairman of the Board,	2002	395,200		15,432		300,000		1,353
Chief Executive Officer and President								
Ronald D. Gunn, M.B.A., M.S. (6)	2004	261,875	65,469					597
	2003	190,900	57,270	203		100,000		438
Executive Vice President and Chief Operating Officer	2002	176,800						370
Andreas Sommer, Ph.D. (7)	2004	260,000	39,000	5,057				
	2003	260,000	26,000	4,165				2,170
Chief Scientific Officer	2002	260,000		5,471		100,000		2,170
Kevin P. Tully, C.G.A. (8)								
Treasurer, Controller and	2004	176,800	44,200					851
	2003	176,800	35,360	203		100,000		851
Principal Financial Officer	2002	164,642				100,000		555
Philip J. Young (9)	2004	173,295	43,324	239,063		250,000		548
Chief Business Officer and								
Executive Vice President,								
Commercial Operations								

(1) Except as disclosed in the table, there was no other cash compensation, long-term incentive plan or restricted stock award that required disclosure.

(2) Includes amounts earned but deferred at the election of the executive, such as salary deferrals under Insmed s 401(k) plan.
(3) Amounts in this column reflect the aggregate annual bonuses that were earned for such fiscal year.
(4) Dr. Allan s other annual compensation for the periods indicated reflects the personal use of a vehicle provided by Insmed and, for 2003, includes $203 given to all employees by the Company as a holiday gift. Dr. Sommer s other annual compensation for the periods indicated includes compensation related to the cost of a medical reimbursement program provided by Insmed and, for 2003, includes $203 given to all employees by the Company as a holiday gift. Mr. Gunn s and Mr. Tully s other annual compensation for 2003 relates to a holiday gift given to all employees by the Company. Mr. Young s other annual compensation related to relocation expenses paid by Insmed on his behalf.
(5) Dr. Allan s, Mr. Gunn s, Dr. Sommer s, Mr. Tully s and Mr. Young s other compensation for 2002, 2003 and 2004 relates to life insurance premiums for coverage in excess of $50,000.

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(6) Mr. Gunn was named Executive Vice President and Chief Operating Officer effective February 1, 2004.
(7) Dr. Sommer joined Insmed on August 1, 2000. He was named an executive officer effective March 4, 2004.
(8) Mr. Tully was named an executive officer effective January 30, 2002.
(9) Mr. Young joined Insmed on April 7, 2004 and was named an executive officer on May 5, 2004.

Director Compensation

Our non-employee directors receive an annual director s fee of $15,000 plus $2,000 and reimbursement of expenses for each meeting of the Board attended in person, $1,000 for each Compensation and Nominations and Governance Committee meeting attended in person, $1,500 for each Audit Committee attended in person and $500 for each meeting attended telephonically. In addition, each non-employee director receives an option to purchase 25,000 shares of Insmed Common Stock upon initial election to the Board and options to purchase 17,500 shares of Insmed Common Stock annually, which options vest one year from the date of grant if the director attends at least 75% of the Board meetings in the preceding fiscal year. Directors who are officers or employees of Insmed do not receive any additional compensation for their services as directors.

Change In Control Arrangements

We have entered into Change in Control Agreements with Dr. Allan, Mr. Gunn, Dr. Sommer, Mr. Tully and Mr. Young, which entitled those executive officers to receive additional benefits in the event of their termination following a change in control of Insmed. We believe that the existence of these potential benefits will benefit Insmed by discouraging turnover and causing such executives to be more able to respond to the possibility of a change in control without being influenced by the potential effect of a change in control on his job security.

For purposes of these agreements, the term change in control generally includes:

(a) the acquisition by another person of beneficial ownership of 40% or more of Insmed Common Stock;

(b) a proxy contest that results in the replacement of 50% or more of the members of Insmed s Board;

(c) a merger after which Insmed s stockholders own less than 60% of the surviving corporation s stock; or

(d) approval by Insmed s stockholders of a complete liquidation or dissolution of Insmed.

If, during the one-year period following a change in control, Insmed or its successor terminates the executive s employment other than for cause or the executive voluntarily terminates employment for after the executive s compensation or duties are changed in any material respect from what they were immediately prior to the change in control, the executive shall receive a lump-sum cash payment equal to the sum of the executive s highest annual salary rate while an employee of Insmed plus a prorated maximum potential bonus. All stock options then held by the executive remain exercisable for the term of the option period set forth in his option agreement(s) and any restricted stock held by the executive remains subject to the restrictions set forth in his restricted stock agreement. In addition, Insmed shall continue to provide to the executive health, dental, long-term disability, life insurance, continuation of D&O insurance, and the other fringe benefits that the executive received prior to termination.

Compensation Committee Interlocks And Insider Participation

The following persons served on our Compensation Committee during the fiscal year ended December 31, 2004: Dr. Sharoky (Chairman), Mr. Condon and Dr. Engelsen. Neither Dr. Sharoky, Mr. Condon nor Dr. Engelsen is or has ever been an officer or employee of Insmed or any of our subsidiaries.

Compensation Committee Report

This report of the Compensation Committee (the Committee) of the Board describes the objectives of Insmed s executive compensation program, the various components of the program, and explains the basis on which compensation determinations for the fiscal year ended December 31, 2004 were made by the Committee.

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Overall Objectives of Executive Compensation Programs

The Committee s guiding philosophy is to establish executive compensation policies that are linked to the sustained creation of shareholder value. The following objectives serve as the guiding principles for all compensation decisions:

provide a competitive total compensation opportunity that will enable Insmed to attract, retain and motivate highly qualified executives;

align compensation opportunities with shareholder interests by making the executive compensation program highly sensitive to Insmed s performance, which is defined in terms of milestones associated with achieving long-term profitability and creating shareholder value; and

provide a strong emphasis on equity-based compensation and equity ownership, creating a direct link between shareholder and management interests.

Compensation Program Components

The Committee believes that the total compensation opportunity available to members of management should consist of base salary, annual bonuses and stock options, with each component geared to the median of the market for all positions in the aggregate. Individuals may be compensated above or below the median of the marketplace based on Insmed s performance and on considerations of individual performance and experience. The Committee considers all elements of the program when setting compensation levels.

The Committee periodically meets individually with members of management in order to assess progress toward meeting objectives set by the Board for both annual and long-term compensation.

The Committee utilizes compensation surveys to aid in the determination of competitive levels of executive pay. The surveys include companies that are larger and smaller than Insmed. Some surveys are limited to companies in the biotechnology business. The Committee also utilizes executive compensation information compiled from the proxy statements of other biotechnology companies. References to the market in this report refer to these survey and proxy data.

Base Salaries

Base salaries are determined in accordance with the responsibilities of each officer, median market data for the position and the officer s performance achieving corporate goals. The Committee considers each of these factors but does not assign a specific value to each factor. Furthermore, a subjective element is acknowledged in evaluating the officer s overall span of responsibility and control. Total compensation for Insmed s officers is believed to be generally in line with the median of the market as described above.

Annual Bonuses

The Committee reviews annual bonuses in conjunction with senior management. The compensation committee has the authority to grant annual bonuses of up to 50% of the CEO s annual salary and up to 35% of individual officers annual salaries. Awards are based on an evaluation of the performance, level of responsibility and leadership of the individual in relation to overall corporate results. For the fiscal year ended December 31, 2004, annual bonuses of 15% to 25% were awarded to officers based on the attainment by individuals of specific objectives necessary for Insmed to achieve its business plan.

Stock Options and Restricted Awards

The Committee believes strongly that equity based awards are an integral part of total compensation for officers and certain key managers with significant responsibility for Insmed s long-term results. Stock options

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that are tied to corporate performance provide an effective means of delivering incentive compensation and also foster stock ownership on the part of management.

The Stock Incentive Plan:

- authorizes the granting of stock options, SARs, performance shares, restricted stock and other incentive awards, all of which may be made subject to the attainment of performance goals established by the Committee;
- provides for the enumeration of the business criteria on which an individual s performance goals are to be based; and
- establishes the maximum share grants or awards (or, in the case of incentive awards, the maximum compensation) that can be paid to a Stock Incentive Plan participant.

In the fiscal year ended December 31, 2004, incentive awards of stock options and performance shares were made in accordance with the performance-based focus of the Stock Incentive Plan.

Discussion of 2004 Compensation for the Chief Executive Officer

Dr. Geoffrey Allan s base salary as Chief Executive Officer was not increased in the fiscal year ended December 31, 2004, and remained at $395,200, the same level as fiscal years ended December 31, 2003 and 2002. The Committee intends base salary to provide Dr. Allan with a level of stability and certainty each year and intends that this particular component of compensation not be affected to any significant degree by company performance factors. The committee awarded Dr. Allan a bonus for 2004 of $98,800 in recognition of the leadership that Dr. Allan has shown in managing the business of the company, raising equity and focusing on maximizing long-term value for our shareholders.

Deductibility of Compensation

The Committee has carefully considered Section 162(m) of the Internal Revenue Code of 1986, as amended, which provides certain criteria for the tax deductibility of compensation in excess of $1 million paid to our executive officers. The Committee believes it is in Insmed s best interests and that of its shareholders to comply with the requirements of Section 162(m), but the Committee intends to preserve the flexibility to reward executives consistent with Insmed s pay philosophy for each compensation element. The Committee intends that grants of options, awards of performance shares, restricted stock and other incentive awards under the Stock Incentive Plan comply with the requirements of Section 162(m).

THE COMPENSATION COMMITTEE

Melvin Sharoky, M.D., Chairman

Kenneth G. Condon, C.P.A., C.F.P., M.B.A.

Steinar Engelsen, M.D.

March 11, 2005

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Performance Graph

The following graph compares cumulative returns for Insmed, the Nasdaq Market Index and the Nasdaq Pharmaceutical Index since June 1, 2000, the day Insmed Common Stock began trading publicly. The comparison assumes $100 was invested on June 1, 2000 and dividends were reinvested.

Date	Insmed	NASDAQ Market Index	NASDAQ Pharmaceutical Index
June 1, 2000	$ 100.00	$ 100.00	$ 100.00
December 29, 2000	21.02	72.57	113.65
June 29, 2001	54.48	64.13	105.34
December 31, 2001	23.15	58.05	96.52
June 28, 2002	8.48	44.13	60.03
December 31, 2002	2.72	40.42	59.36
June 30, 2003	16.30	49.20	83.53
December 31, 2003	18.00	60.89	89.52
June 30, 2004	13.58	62.55	107.27
December 31, 2004	13.33	66.74	111.77

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Option Grants in Fiscal Year Ended December 31, 2004

The following tables show the stock options granted to the Company s chief executive officer, each executive officer, each non-employee director and all other employees (other than executive officers) during the fiscal year ended December 31, 2004. The Company did not grant any stock appreciation rights (SARs) during the fiscal year ended December 31, 2004.

	INDIVIDUAL GRANTS				POTENTIAL REALIZABLE VALUE AT ASSUMED ANNUAL RATES OF STOCK PRICE APPRECIATION FOR OPTION TERM	
Name	Number of Securities Underlying Options Granted (#)	Name	Number of Securities Underlying Options	Name	Number of Securities Underlying Options Granted (#)	Name
Geoffrey Allan, Ph.D.						
Ronald D. Gunn, M.B.A., M.S.						
Andreas Sommer, Ph.D.						
Kevin P. Tully, C.G.A.						
Philip J. Young	150,000(1)	15.4%	3.00	4/7/2010	153,043	347,202
	100,000(2)	10.2%	1.30	8/10/2013	71,673	176,533

(1) Options vest and become exercisable in equal annual increments over a four year period.
(2) These shares will vest in 25,000 shares increments upon attaining certain milestones established by the Company relating to the commercialization of one of our principal drug products, SomatoKine®, provided that these milestone-based options will vest on August 10, 2011 (seven years from Date of Grant), if not sooner vested.

Name	Number of Securities Underlying Options Granted (#)	Exercise or Base Price($/sh.)
All executive officers	380,000	2.22
All non-employee directors	87,500	2.70
All employees (excluding Executive Officers)	438,500	1.94

Aggregated Option Exercises in Fiscal Year Ended December 31, 2004 and Fiscal Year-End Option Values

The following table shows the stock options exercised by the named executive officers during the fiscal year ended December 31, 2004 and the number and value of all unexercised options held by the named executive officers at December 31, 2004.

Name	Shares Acquired on Exercise (#)	Value Realized ($)	Number of Securities Underlying Unexercised Options at Fiscal Year-End(#)		Value of Unexercised In-the-Money Options at Fiscal Year-End($)	
			Exercisable	Unexercisable	Exercisable	Unexercisable
Geoffrey Allan, Ph.D.			601,554	435,947	145,005	109,845
Ronald D. Gunn, M.B.A., M.S.			198,425	206,251	59,874	73,230
Andreas Sommer, Ph.D.			248,749	193,751	21,770	73,230
Kevin P. Tully, CGA			113,749	116,251	61,403	91,597
Philip J. Young				250,000		90,000

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ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth the beneficial ownership of Insmed Common Stock as of March 11, 2005 by all directors, nominees and executive officers named in the Summary Compensation Table contained in this Proxy Statement. The table also shows the beneficial ownership of all directors and executive officers as a group.

Name of Beneficial Owner	Aggregate Number of Shares Beneficially Owned (1)	Percent of Class
Geoffrey Allan, Ph.D. (2)	1,713,259	3.7%
Kenneth G. Condon, C.P.A., C.F.P., M.B.A. (3)	521,776	1.2%
Graham K. Crooke, MB.BS (4)	894,490	2.0%
Steinar J. Engelsen, M.D. (5)	105,625	*
Ronald D. Gunn, M.B.A., M.S. (6)	303,405	*
Melvin Sharoky, M.D. (7)	389,600	*
Andreas Sommer, Ph.D. (8)	319,932	*
Kevin P. Tully, C.G.A. (9)	231,034	*
Randall W. Whitcomb, M.D. (10)	113,500	*
Philip J. Young (11)	42,179	*
All directors and executive officers as a group (10 persons) (12)	4,634,800	10.2%

* Denotes ownership of less than 1% of the outstanding shares of Insmed Common Stock.

(1) Except as indicated otherwise in the footnotes, shares shown as beneficially owned are those to which the individual has sole voting and investment power. Shares subject to options that are exercisable within 60 days of March 11, 2005, are deemed to be outstanding and to be beneficially owned by the person holding such options for the purpose of computing the percentage ownership of such person, and of the directors and executive officers as a group, but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

(2) Includes 711,795 shares issuable upon exercise of options, which options are exercisable within 60 days of March 11, 2005.

(3) Mr. Condon, a director of Insmed, currently has the right to purchase 57,500 shares upon exercise of options. The number of shares listed opposite Mr. Condon s name also includes 444,463 shares owned by Boston University Nominee Partnership, of which he is a partner, and 15,750 shares owned by Trustees of Boston University.

(4) Dr. Crooke, a director of Insmed, has the right to purchase 157,500 shares upon exercise of options. The number of shares listed opposite Dr. Crooke s name also includes 686,990 shares owned by Concord Partners III, LP (formerly Dillon Read Venture Partners III LP). Dr. Crooke has an ownership interest (but not a management interest) in Concord Associates III, LLC which is the sole general partner of Concord Partners III, LP.

(5) Dr. Engelsen, a director of Insmed, currently has the right to purchase 57,500 shares upon exercise of options.

(6) Includes 263,331 shares issuable upon exercise of options, which options are exercisable within 60 days of March 11, 2005.

(7) Dr. Sharoky, a director of Insmed, currently has the right to purchase 62,500 shares upon exercise of options. The number of shares listed opposite Dr. Sharoky s name includes 210 shares which are owned by his minor son 620 shares which are owned by his minor daughter and 3,600 shares which are owned by his spouse.

(8) Includes 313,331 shares issuable upon exercise of options, which options are exercisable within 60 days of March 11, 2005.

(9) Includes 132,082 shares issuable on exercise of options, which options are exercisable within 60 days of March 11, 2005.

(10) Dr. Whitcomb, a director of Insmed, currently has the right to purchase 62,500 shares upon exercise of options. The number of shares listed opposite Dr. Whitcomb s name includes 21,000 shares that are owned by the Randall W. Whitcomb Living Trust. Dr. Whitcomb and his spouse, Rita K. Whitcomb, are trustees of the Randall W. Whitcomb Living Trust.

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(11) Includes 37,500 shares issuable on exercise of options, which options are exercisable within 60 days of March 11, 2005.
(12) Represents the sum of the shares beneficially owned by all directors, nominees and executive officers named in the table above.

Equity Compensation Plan Information

The following table presents information as of December 31, 2004, with respect to compensation plans under which shares of Insmed Common Stock are authorized for issuance.

Plan Category	Number of Securities to Be Issued upon Exercise of Outstanding Options, Warrants and Rights	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans(1)
Equity Compensation Plans Approved by Shareholders:			
2000 Stock Incentive Plan	4,864,425	$ 3.70	777,740(2)