INSMED INC
Form 424B5
March 06, 2006
Table of Contents

Filed Pursuant To Rule 424(b)(5)
Registration Statement 333-131535

The information in this prospectus supplement is not complete and may be changed. This prospectus supplement and the attached prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Prospectus Supplement

(To Prospectus Dated February 14, 2006)

20,000,000 Shares

Common Stock

Insmed Incorporated is offering 20,000,000 shares of its common stock.

Our common stock is quoted on The Nasdaq National Market under the symbol INSM. On March 3, 2006, the last reported sale price of our common stock on The Nasdaq National Market was $2.37 per share.

See Risk Factors beginning on page S-7 of this prospectus supplement to read about factors you should consider before buying shares of our common stock. You should read this prospectus supplement and the accompanying prospectus carefully before you make your investment decision.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	$	$
Underwriting discount	$	$
Proceeds, before expenses, to Insmed Incorporated	$	$

We have granted the underwriters the right to purchase up to 3,000,000 additional shares at the public offering price per share, less the underwriting discount, within 30 days of this prospectus supplement to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment on or about March , 2006.

LAZARD CAPITAL MARKETS **C.E. UNTERBERG, TOWBIN**

The date of this prospectus supplement is , 2006.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

Prospectus

We have applied for trademark registrations for Insmed and IPLEX. This prospectus supplement and the accompanying prospectus also contain other trademarks, service marks and trade names that are the property of other parties.

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

You should read this prospectus supplement along with the accompanying prospectus carefully before you invest in our common stock. Both documents contain important information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained or incorporated by reference in the accompanying prospectus. You should rely only on the information provided in this prospectus supplement and the accompanying prospectus or incorporated by reference in the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with different information. We are not, and the underwriters are not, making an offer to sell our common stock in any jurisdiction where the offer or sale is not permitted.

You should not assume that the information contained in this prospectus supplement and the accompanying prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on the date subsequent to the date of the document incorporated by reference. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained or incorporated by reference in the accompanying prospectus, on the other hand, the information contained in this prospectus supplement shall control.

Table of Contents

SUMMARY

This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary may not contain all of the information that is important to you. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the Risk Factors section contained on page S-7 of this prospectus supplement, before deciding to invest in our common stock.

About Insmed

Our Business

Insmed Incorporated is a biopharmaceutical company focused on the development and commercialization of drugs to treat metabolic diseases and endocrine disorders within niche markets that have unmet medical needs. Currently, our development and commercial activities involve drugs that modulate Insulin-like Growth Factor-1, or IGF-1, activity in the human body. Our lead product, IPLEX (mecasermin rinfabate [rDNA origin] injection), is the only FDA approved, once-daily IGF-1 replacement therapy. IPLEX was approved in December 2005 for the treatment of growth failure in children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone (Severe Primary IGFD). As an Orphan Drug, IPLEX is entitled to seven years of marketing exclusivity in the treatment of Severe Primary IGFD in the United States. We are conducting and plan to pursue further clinical trials in order to expand the label for IPLEX into additional clinical indications.

We are building our own specialty sales force to launch IPLEX in the United States in the second quarter of this year. We believe we can effectively market IPLEX by targeting the top 400 pediatric endocrinologists in the United States who we estimate treat the substantial majority of the approximately 6,000 children who suffer from severe short stature due to Severe Primary IGFD. The positive therapeutic characteristics of IPLEX that we believe will make it a commercial success are:

- IPLEX has demonstrated statistically significant increases in linear growth.
- IPLEX is the only once-daily IGF-1 replacement therapy approved for use in the United States.
- IPLEX may be administered either in the morning or evening.
- IPLEX has demonstrated an acceptable safety profile.

We believe the commercial opportunities for IPLEX are significant and reach beyond our approved indication of Severe Primary IGFD. Subject to completion of additional clinical studies and regulatory approval, the initial approval of IPLEX may offer us an opportunity for label expansion into other indications, most with larger patient populations than Severe Primary IGFD. We are currently conducting Phase II clinical studies in patients with myotonic muscular dystrophy, HIV associated adipose redistribution syndrome and extreme insulin resistance. We also intend to conduct additional clinical studies in other growth disorders associated with IGF-1 deficiency.

We also intend to expand the market for IPLEX by pursuing approvals outside of the United States, including the European Union. We have been granted Orphan Drug Designation by the European Medicines Agency for the Evaluation of Medicinal Products, or the EMEA, for IPLEX in the treatment of primary Growth Hormone Insensitivity Syndrome (Laron Syndrome) or GHIS. Should marketing approval of IPLEX be granted for this indication by the EMEA, as an Orphan Drug, IPLEX will be provided up to 10 years of marketing exclusivity in the European Union. We plan to file for marketing authorization with the EMEA in the third quarter of 2006.

Table of Contents

In addition to our IPLEX development and commercialization programs, we have an oncology program focused on two compounds, INSM-18 and rhIGFBP-3. Our longer-term development efforts are primarily focused on the potential to treat cancers by using these compounds to target growth factors and their receptors. Our small molecule compound, INSM-18, has novel effects on the activity of the IGF-1 and other receptors, such as Her2/Neu, and may lead to the inhibition of growth of various tumors. A Phase I/II clinical study of INSM-18 in refractory prostate cancer patients has been initiated at the University of California, San Francisco School of Medicine. rhIGFBP-3 is a naturally occurring anti-tumor agent normally found in the human bloodstream. Several epidemiological studies have demonstrated that cancer risk increases as levels of rhIGFBP-3 in the blood decrease. A Phase I clinical study to evaluate rhIGFBP-3 safety and tolerance in human volunteers is in progress.

Our Business Strategy

We intend to capitalize on the therapeutic opportunities presented by IPLEX by commercializing it in its approved indication in the United States and extending the use of IPLEX in other indications and other geographic markets. We also intend to develop, seek regulatory approval of and commercialize other drugs for the treatment of other metabolic diseases and endocrine disorders with unmet medical needs. Key elements of our strategy include:

Launch IPLEX commercially in 2006 with our own specialty sales force. We are building a sales and marketing force to target approximately 400 U.S.-based pediatric endocrinologists who we estimate treat the substantial majority of children with Severe Primary IGFD.

Develop IPLEX in additional non-growth disorder indications. We have initiated studies in myotonic muscular dystrophy (estimated U.S. patient population is 40,000), HIV associated adipose redistribution syndrome (estimated U.S. patient population is at least 80,000) and extreme insulin resistance.

Expand the Severe Primary IGFD indication to other growth disorders related to IGF-1 deficiency. There are a number of growth disorders related to IGF-1 deficiency other than Severe Primary IGFD which may permit us to expand the U.S. market for IPLEX from 6,000 children to approximately 35,000 children.

Establish a commercialization strategy for IPLEX outside the United States. In addition to pursuing approvals for IPLEX outside of the United States, we will either build our own European sales and marketing team or explore European partnering opportunities.

Develop Oncology Portfolio. We will continue to conduct clinical studies of INSM-18 and rhIGFBP-3 for the treatment of cancer and evaluate opportunities to initiate Phase II clinical studies for these products.

Product Pipeline

Name	Indication	Status
IPLEX	Growth Failure associated with Severe Primary IGFD	FDA Approved
IPLEX	Myotonic Muscular Dystrophy	Phase II
IPLEX	HIV Associated Adipose Redistribution Syndrome (HARS)	Phase II
IPLEX	Extreme Insulin Resistance	Phase II
IPLEX	Growth Failure associated with IGF-1 Deficiency (Noonan Syndrome)	Phase II Planned
INSM-18	Refractory Prostate Cancer	Phase I/II
rhIGFBP-3	Cancer	Phase I

Table of Contents

Risks Affecting Us

Our business is subject to numerous risks as discussed more fully in the section entitled Risk Factors immediately following this prospectus supplement summary on page S-7. We are involved in significant patent litigation matters which if determined adversely would have a material adverse effect on our business, financial condition and results of operations. We may be unable, for many reasons, including those that are beyond our control, to implement our current business strategy. We have received regulatory approval for only one of our products and have not launched, or earned commercial revenues from, any of our products. If we do not successfully commercialize IPLEX or another product we will not generate the revenue necessary to fund our continuing efforts to develop and commercialize our drug candidates. In addition, the reported results of our early-stage clinical trials may not be indicative of results achieved in later-stage, larger clinical trials. As of December 31, 2005, we had an accumulated deficit of approximately $254.7 million. We expect to continue to incur significant losses over the next several years, and we may never become profitable.

Corporate Information

Insmed was incorporated in the Commonwealth of Virginia on November 29, 1999. Our principal executive offices are located at 4851 Lake Brook Drive, Glen Allen, Virginia 23060 and our phone number is (804) 565-3000. Our Internet address is www.insmed.com. We make available on our Internet website free of charge a link to our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports as soon as practicable after we electronically file such material with the SEC. Information contained on our website is not incorporated into this prospectus supplement or the accompanying prospectus, and is not a part of this prospectus supplement or the accompanying prospectus.

Table of Contents

THE OFFERING

Common stock offered	20,000,000 shares
Common stock to be outstanding after the offering	86,525,792 shares
Use of proceeds	Working capital and other general corporate purposes, including funding our clinical studies and manufacturing costs. See Use of Proceeds on page S-26
Risk Factors	See Risk Factors beginning on page S-7 of this prospectus and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should consider before buying shares of our common stock.
The Nasdaq National Market Symbol	INSM

The number of shares of common stock to be outstanding after this offering is based on 66,525,792 shares outstanding as of December 31, 2005. The number of shares of common stock offered and to be outstanding after this offering excludes:

- 3,000,000 shares of common stock that the underwriters have a right to purchase from us to cover over-allotments;
- 22,550,332 shares issuable upon the exercise of stock options and warrants outstanding as of December 31, 2005 and having a weighted average exercise price of $2.03 per share;
- 8,832,432 shares issuable upon the conversion of convertible notes with an aggregate principal amount of $11,438,000 outstanding as of December 31, 2005; and
- 2,736,095 shares available for issuance under our equity incentive plans as of December 31, 2005.

Between January 1, 2006 and February 28, 2006, 4,189,189 shares of common stock were issued upon the conversion of convertible notes with an aggregate principal amount of $5,425,000, and warrants and options were exercised for 6,405,921 shares of common stock. None of these 10,595,110 shares issued upon conversion of convertible notes or exercise of warrants and options are included in the number of shares of common stock listed above as outstanding after the offering.

Table of Contents

SELECTED FINANCIAL DATA

The following selected financial data are derived from the consolidated financial statements of Insmed Incorporated which have been audited by Ernst & Young LLP, our independent registered public accounting firm. Ernst & Young LLP s report on the consolidated financial statements for the year ended December 31, 2005, which is incorporated by reference herein, includes an explanatory paragraph which describes an uncertainty about Insmed Incorporated s ability to continue as a going concern. The historical results presented below are not necessarily indicative of the results to be expected in any future period. It is important that you read this information together with Management s Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and notes to those consolidated financial statements incorporated by reference in this prospectus supplement from our Annual Report on Form 10-K for the year ended December 31, 2005.

	Year Ended December 31,		
	2003	2004	2005
	(in thousands, except per share data)		
Historical Statement of Operations Data:			
Revenues	$ 150	$ 137	$ 131
Operating expenses:			
Research and development	7,140	23,260	21,835
General and administrative	3,477	4,242	5,730
Operational restructuring charge			
Goodwill write-off			
Purchased research and development			
Stock compensation	119		
Total operating expenses	10,736	27,502	27,565
Operating loss	(10,586)	(27,365)	(27,434)
Interest income, net	288	222	752
Interest expense		(60)	(14,247)
Loss before income taxes	(10,298)	(27,203)	(40,929)
Income tax expense			
Net loss	(10,298)	(27,203)	(40,929)
Basic and diluted net loss per share	(0.29)	(0.69)	(0.84)
Weighted average shares	35,600	39,160	48,742
Historical Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 29,526	$ 9,222	$ 18,835
Total assets	29,812	13,011	22,870
Stockholders equity	26,220	7,235	10,529

Table of Contents

RISK FACTORS

You should consider carefully the following risk factors, together with all of the other information included in this prospectus supplement or incorporated by reference into this prospectus supplement. 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.

Until recently, we have been focused solely on drug 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 preclinical testing and clinical studies 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, distribution 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, 2005, our accumulated deficit was $254.7 million. For the year ended December 31, 2005 our consolidated net loss was $40.9 million.

We have only one drug that has been approved for commercial sale by the FDA, IPLEX , and we are in the earlier stages of researching and developing two other drug candidates, INSM-18 and rhIGFBP-3. Until we have had an opportunity to establish IPLEX as a commercially viable product or complete the development and commercialization of our other drug candidates, we cannot predict our future revenue with any degree of certainty.

For these and other reasons, our independent registered public accounting firm believes that there is substantial doubt that we will be able to continue as a going concern. If we do not continue as a going concern our investors will likely lose all of their investments.

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

Third parties have claimed that we are infringing or have misappropriated their proprietary rights and we can give no assurances that other third parties will not claim that we and our licensees who develop and distribute our products, are infringing their proprietary rights. It is difficult to predict with any certainty the outcome of any legal proceeding. If a court determines that we may not manufacture or sell our products or use our processes without having obtained 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.

With respect to any infringement claim asserted by a third party, we can give no assurances that we will 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. In the event of a successful claim against us for infringement or misappropriation of a third party s proprietary rights, we may be required to:

- pay damages, including up to treble damages, and the other party s attorneys fees, which may be substantial;
- cease the development, manufacture, marketing and sale of products or use of processes that infringe the proprietary rights of others;

expend significant resources to redesign our products or our processes so that they do not infringe the proprietary rights of others, which may not be possible;

redesign our products or processes to avoid third party proprietary rights, we may suffer significant regulatory delays associated with conducting additional clinical trials or other steps to obtain regulatory approval; and

obtain one or more licenses arising out of a settlement of litigation or otherwise from third parties for the infringed proprietary rights, which may not be available to us on acceptable terms or at all.

In this regard, we note that on December 20, 2004, Tercica, Inc. and Genentech, Inc. filed a complaint against Avecia Limited and us in the United Kingdom at the High Court of Justice, Chancery Division, Patents Court alleging infringement of EP patent No. 571,417, or the 417 patent. The 417 patent has claims directed to particular uses of a combination of IGFBP-3 and IGF-1. In the complaint, Tercica 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. In May 2005, we filed for summary judgment to dismiss the complaint. The motion for summary judgment was denied. A trial date in this litigation has not been set.

In addition, on December 23, 2004, Genentech and Tercica sued us for infringement of U.S. Patent Nos. 5,187,151 and 6,331,414 in the United States District Court for the Northern District of California. These patents are directed to certain methods of using rhIGF-1/rhIGFBP-3 and methods of producing rhIGF-1, respectively. On February 16, 2005, Tercica filed an amended complaint, adding an infringement allegation against us with respect to U.S. Patent No. 5,528,287, or 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 the same. Genentech and Tercica claim that the production or use of IPLEX, a complex of rhIGF-1/rhIGFBP-3, will infringe these patents. We moved to dismiss the amended complaint for lack of jurisdiction and on other grounds. At a hearing on the motion on April 15, 2005, the court granted our motion and dismissed the case with leave for plaintiffs to refile the complaint. A second amended complaint was filed on April 22, 2005 by Genentech and Tercica against us that, among other things added Celtrix Pharmaceuticals, our wholly-owned subsidiary, as a defendant. We moved to dismiss the portion of the second amended complaint that relates to the 287 patent. On June 29, 2005, the Court denied our motion to dismiss. On July 14, 2005, we filed our answer and counterclaims, in which we denied infringement and sought a declaratory judgment that the asserted patents are not infringed, are invalid, and/or are unenforceable. The reply to the counterclaims by Genentech and Tercica was filed on August 5, 2005. On October 17, 2005, Tercica and Genentech filed a third amended complaint adding Insmed Therapeutic Proteins, our wholly-owned subsidiary, as a defendant. The answer and counterclaims in response to the third amended complaint were filed by us on October 27, 2005. Briefing on patent claim construction issues and summary judgment motions is set to be completed by May 5, 2006, with a claim construction hearing scheduled for May 19, 2006. Discovery is ongoing and a trial date is scheduled for November 2006.

On May 27, 2005, Genentech and Tercica filed a motion for preliminary injunction seeking an order barring us, until trial, from making, using or selling the drug called SomatoKine, (now known as IPLEX) with respect to its allegations of infringement of U.S. Patent Nos. 6,331,414 and 5,187,151, and requesting that we be required to share any Orphan Drug Exclusivity it obtains with Tercica. We filed an opposition to the motion for a Preliminary Injunction on June 10, 2005. On June 16, 2005, Genentech and Tercica withdrew their motion for a preliminary injunction, but reserved the right to refile the motion for a preliminary injunction. We cannot predict whether Genentech and Tercica will seek a preliminary injunction at another time.

We cannot predict with certainty the outcome of proceedings involving Tercica and Genentech. The claim construction ruling and summary judgment rulings to be issued by the court, which could occur in the next few months, could have an adverse impact on our position in this proceeding, including by narrowing or limiting our defenses. An adverse ruling after trial on any of the claims alleged would have a material adverse effect on our business, financial condition and results of operations and would lead to some or all of the consequences described above, such as damages and the requirement that we cease manufacture and sale of IPLEX unless we

Table of Contents

can obtain a license or develop or acquire alternative products or processes that do not infringe the patents, which may not be available on commercially favorable terms, if at all. Further, we may have an obligation to indemnify distributors of IPLEX and other third parties. In addition, if such adverse ruling requires us to cease the manufacture and sale of IPLEX and we are unable to raise the capital (in addition to the capital raised in this offering) that would be necessary to conduct the clinical trials necessary to obtain regulatory approval of our other product candidates, we could be forced to curtail our development programs and possibly to cease operations altogether.

These proceedings have required a substantial diversion of financial and personnel resources from operations. Further, defending any future patent infringement claims will also require that we divert financial and personnel resources from operations and may expose us to liabilities for costs or other damage awards.

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 our patents; and
- refrain from infringing the patents of others, both domestically and internationally.

Our patent positions are highly uncertain and involve complex legal and factual questions, 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 resulting from our research and development activities that have significant potential commercial value. Nevertheless, due to the inherent uncertainty of the patent process, 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.

Third parties have claimed that we are infringing or have misappropriated their proprietary rights. We can give no assurance that other third parties will not make similar claims. Various third parties have obtained, and are attempting to obtain, patent protection relating to the production and use of our approved product and product candidates. 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 IPLEX or any other product. We can give no assurances that such patents can be avoided, invalidated or licensed.

If third parties successfully bring legal action against us or our licensees claiming patent or other intellectual property infringement, in addition to any potential liability for damages, including compensatory damages and treble damages, a court could require us and/or our licensees to cease using any infringing processes or manufacturing and selling any infringing products. Such a result would likely have a material adverse effect on our business, financial condition and results of operations. Any such claim, with or without merit, could result in costly litigation, require us to pay significant settlement amounts or 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.

Furthermore, litigation with any third party, even if the allegations are without merit, would likely be expensive and time-consuming and divert management s attention.

Any conclusions we may have reached regarding non-infringement and invalidity are based in part on a review of publicly available databases and other information. There may be information not available to or otherwise not reviewed by us that might change our conclusions. Moreover, as described above, the scope and validity of patent claims are determined based on many facts and circumstances, and in a litigation a court may reach a different conclusion on any given patent claim than the conclusions that we have reached.

Table of Contents

We note that third parties with significant financial resources, including Genentech, Inc., Novartis and Chiron Corporation hold United States and/or foreign patents possibly directed to the composition, production and/or use of rhIGF-1, rhIGFBP-3, IPLEX and/or recombinant proteins. We can provide no assurance that any one of these third parties will not assert an infringement action against us that may adversely affect our ability to make, use or sell our products.

We may have to undertake costly litigation to enforce any patents issued or licensed to us or to determine the scope and validity of another party s proprietary rights. We 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 result in the invalidation of our patents and could otherwise materially adversely affect our business, financial condition and results of operations.

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

Even if we are successful in developing and obtaining approval for our drug candidates, there are numerous circumstances that could prevent the successful commercialization of the products such as:

- the regulatory approvals of our products are delayed or we are required to conduct further research and development of 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;
- we are required to allocate available funds to litigation matters;
- 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;
- we are unsuccessful in defending against patent infringement claims being brought against us our products or technologies; or
- we are unable to obtain reimbursement for our product 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.

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.

Now that the FDA has permitted us to commence commercial sales of IPLEX, we must establish capabilities to complete the commercial sale, marketing and distribution of IPLEX. These are areas in which we

Table of Contents

have no experience. To market IPLEX or any of our products directly, we must develop a marketing and sales force with technical expertise and with supporting distribution capability. We may engage a pharmaceutical company with a large distribution system and a large direct sales force to assist us in marketing IPLEX outside the United States or in marketing any of our other products. There can be no assurance that we will successfully establish sales and distribution capabilities or establish third-party sales and distribution arrangements on satisfactory terms, or at all. To the extent we enter into co-promotion, licensing, third-party sales or distribution agreements, 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 approved drug or our drug candidates, if approved for marketing, will achieve market acceptance. If our drugs and drug candidates, once approved, 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 drugs 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 drugs;
- 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 after 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.

In addition, legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us. While we cannot predict the likelihood of any such legislative or regulatory proposals, if the government or an agency adopts such proposals, they could materially adversely affect our business, financial condition and results of operations.

If there are fewer children with Severe Primary IGFD than we estimate, we may not generate sufficient revenues to continue development of other products or to continue operations, or we may not be able to complete our clinical studies.

We estimate that the number of children in the United States with Severe Primary IGFD is approximately 6,000. Our estimate of the size of the patient population is based on our interpretation of published studies. If our interpretation and extrapolation of data from these published studies do not accurately reflect the number of children with Severe Primary IGFD, our assessment of the market may be incorrect and we may not achieve sufficient revenue to continue operations.

Reimbursement policies and changes in the health care system may adversely affect the sale of our current and future products or our ability to obtain an adequate level of reimbursement or acceptable prices for our current and future products.

Our ability to earn sufficient returns on IPLEX or our other products, if and when such products are approved and ready for marketing, will depend in part on the extent to which reimbursement for our products and

Table of Contents

related treatments will be available from government health administration authorities, private health coverage insurers, managed care organizations and other third-party payers. If we fail to obtain appropriate reimbursement, it could prevent us from successfully commercializing our future products.

There have been and continue to be efforts by governmental and third-party payers to contain or reduce the costs of health care through various means, including limiting coverage and the level of reimbursement. We expect that there will continue to be a number of legislative proposals to implement government controls and other reforms to limit coverage and reimbursement. The announcement of these proposals or reforms could impair our ability to raise capital. The adoption of these proposals or reforms could impair our operations and financial condition.

Additionally, third-party payers, including Medicare, are increasingly challenging the price of medical products and services and are limiting the reimbursement levels offered to consumers for these medical products and services. If purchasers or users of our future products are not able to obtain adequate reimbursement from third-party payers for the cost of using these products, they may forego or reduce their use. Significant uncertainty exists as to the reimbursement status of newly approved health care products and whether adequate third-party coverage will be available.

We cannot provide any assurance that third-party payers will provide adequate reimbursement, if any, for IPLEX.

We cannot be certain that we will obtain additional 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 preclinical studies and clinical studies, 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 preclinical and clinical data, manufacturing information regarding the process and facility, scientific data characterizing our product and other supporting data to the regulatory authorities in order to establish its safety and effectiveness. This process is also complex, lengthy, expensive, resource intensive and uncertain. We have limited experience in filing and pursuing applications necessary to gain these regulatory approvals.

Data submitted to the regulators is subject to varying interpretations that could delay, limit or prevent regulatory agency approval. We may also encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a drug and/or the period required for review of any application for regulatory agency approval of a particular product. Delays in obtaining regulatory agency approvals could adversely affect the marketing of any drugs that our collaborative partners or we develop. Such delays could impose costly procedures on our collaborative partners or our activities, diminish any competitive advantages that our collaborative partners or we may attain and adversely affect our ability to receive royalties, any of which could materially adversely affect our business, financial condition and results of operations.

We are currently conducting a Phase III clinical trial of IPLEX in patients with Severe Primary IGFD and plan to include the data in a MAA submission to the EMEA. We must receive approval of these applications before we can market IPLEX in certain countries outside of the United States.

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 and for commercialization is essentially the same as the new drug product produced. We have had several discussions with the FDA and intend to have discussions with foreign regulatory agencies regarding our Phase III clinical study and this comparability analysis. We believe we understand what is required to satisfy the EMEA. We plan to submit this

Table of Contents

data to the appropriate regulatory authorities as part of the regulatory process. If we do not properly understand what is required to satisfy regulatory authorities or 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.

Regulatory authorities have substantial discretion in the approval of our drug candidates 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 IPLEX. If the EMEA does not accept or approve our application, it may require that we conduct additional clinical, preclinical 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 the 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. Further, any 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 the results of our Phase III clinical trial for IPLEX do not continue to support the approval of IPLEX 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 FDA and/or EMEA approvals or such approvals may be substantially delayed or withdrawn. Any of these events might prevent us from selling IPLEX in its approved indication or from expanding the market for IPLEX, either of which would materially adversely affect our business, financial condition and results of operations.

Even if we obtain approval for our products in the United States or the European Union, we cannot be certain that we will obtain any regulatory approvals in other 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 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 the EMEA does not ensure approval by the regulatory authorities of other countries. The failure to obtain such approvals may materially adversely affect our business, financial condition and results of operations.

We are currently a defendant in a civil action in which we are accused of deceptive promotional statements and unfair business practices. An unfavorable settlement or judgment in this action could harm our business and financial condition.

On December 6, 2005, Tercica filed a complaint against us in the United States District Court for the Northern District of California alleging we made deceptive promotional statements and engaged in unfair business practices related to Tercica s drug, Increlex, in violation of the California Business and Professions Code and the Federal Lanham Act. Tercica amended the complaint on December 15, 2005. Tercica is requesting injunctive and monetary relief.

Table of Contents

Although we deny any liability, no assurances can be given as to the outcome of this action. An unfavorable settlement or decision could affect 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. Any liability resulting from this action may exceed our financial resources. The parties have not initiated discovery in this action and no trial date has been set.

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 studies 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.

Currently, we are aware of at least one other company, Tercica, that has received approval from the FDA for a rhIGF-1 product for an indication very similar to the indication for which IPLEX has been approved. Tercica s product was approved for the long term treatment of growth failure in children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone. We believe this indication would include patients with Severe Primary IGFD. Because there are already patients using Tercica s product, the market opportunity for IPLEX may be diminished if doctors who are already prescribing Tercica s product to their patients are unwilling to switch their patients to a different drug. We believe Tercica may also be planning to develop rhIGF-1 for some of the same indications that we plan to pursue with IPLEX.

Growth hormone may also be a competitive product for the treatment of some indications that we may pursue with IPLEX such as HIV associated adipose redistribution syndrome. 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 studies for the use of its growth hormone in pediatric IGF-1 deficiency. We are also aware that Serono is seeking regulatory approval for their growth hormone, Serostim , for the treatment of HIV associated adipose redistribution syndrome, and that Theratechnologies is conducting Phase III studies for a growth hormone releasing agonist 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 preclinical 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 IPLEX.

Table of Contents

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 that are developing products that are intended to target the same IGF-1 pathway as rhIGFBP-3. These companies include ImClone, Amgen, OSI Pharmaceuticals, Bristol-Myers Squibb and Genentech.

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 success 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.

Competitors could develop and gain FDA approval of products containing rhIGF-1, which could adversely affect our competitive position in all indications where we are currently developing IPLEX.

rhIGF-1 manufactured by other parties may be approved for use in other indications in the United States in the future, including myotonic muscular dystrophy, HIV associated adipose redistribution syndrome and severe insulin resistance. In the event there are other rhIGF-1 products approved by the FDA to treat indications other than those covered by IPLEX, physicians may elect to prescribe a competitor s product containing rhIGF-1 to treat the indications for which IPLEX has received and may receive approval. This is commonly referred to as off-label use. While under FDA regulations a competitor is not allowed to promote off-label use of its product, the FDA does not regulate the practice of medicine and as a result cannot direct physicians as to what product containing rhIGF-1 to prescribe to their patients. As a result, we would have limited ability to prevent off-label use of a competitor s product containing rhIGF-1 to treat any diseases for which we have received FDA approval even if it violates our patents and/or we have orphan drug exclusivity for the use of rhIGF-1 to treat such diseases.

If another party obtains Orphan Drug Exclusivity for a product that is essentially the same as a product we are developing in a particular indication, we may be precluded or delayed from commercializing the product in that indication. This may 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. 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 drug may be approved by the FDA for the same orphan indication or disease as long as the drugs are different drugs. As a result, even if our product is approved and receives Orphan Drug Exclusivity, as in the case of our drug IPLEX, the FDA can still approve different drugs for use in treating the same indication or disease covered by our product, which could create a more competitive market for us. For example, the FDA approved Tercica s drug, Increlex , for the treatment of Severe Primary IGFD and granted Tercica s product Orphan Drug Exclusivity. Therefore, Tercica s product will compete with IPLEX for the treatment of Severe Primary IGFD when IPLEX is launched commercially and the value of IPLEX s Orphan Drug Status in this indication will be limited.

Table of Contents

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.

We may not be able to manufacture quantities of IPLEX sufficient to meet market demand, or manufacturing capacity necessary to supply IPLEX, rhIGFBP-3 or INSM-18 for use in clinical studies 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 or successfully implement our own manufacturing capabilities, 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 IPLEX and rhIGFBP-3 bulk drug substance and perform the majority of analytical testing at our manufacturing facility in Boulder, Colorado and utilize contract manufacturers for sterile filtering, filling, finishing, labeling and some analytical testing. We intend to manufacture INSM-18 with contract manufacturers.

In order to meet anticipated commercial and clinical demand for IPLEX and clinical demand for rhIGFBP-3, we plan to implement stepwise changes to our Boulder, Colorado manufacturing facility and manufacturing process beginning this year. We must submit to the FDA information and data pertaining to these changes and the FDA must approve these changes before we will be allowed to use IPLEX or rhIGFBP-3 that is manufactured following implementation of these changes.

There can be no assurance that we will be successful in implementing changes to our manufacturing facility or process for making IPLEX and rhIGFBP-3 or that the FDA will review and approve these changes in a timely manner or at all or that contract manufacturers will have the capacity to produce and test our products. If we are unable to implement the required changes to our manufacturing facility and process or there is a delay in the implementation and approval of these changes, we will be limited to our current manufacturing capacity and would not be able to meet the market or clinical demand which would adversely affect the development and commercialization of IPLEX and rhIGFBP-3. If our contract manufacturers are unable to meet our sterile filtering, filling, finishing, labeling and analytical testing needs, in a way that meets our time and cost parameters, our commercialization of IPLEX and the development and timing of our preclinical and clinical studies may be adversely affected.

In addition, there can be no assurance that an adverse regulatory inspection at our manufacturing facility or contract manufacturer would not impede our commercial supply capability. We have chosen to commercialize IPLEX on our own and this is time consuming, resource intensive and capital intensive. If our facilities and contract manufacturers cannot produce and test our products according to current good manufacturing practices, or cGMP, and pass a cGMP inspection, we may be unable to develop and commercialize our products. This would materially adversely affect our business, financial condition and results of operations.

The available capacity for the manufacture and testing of recombinant proteins that comprise IPLEX is limited. A shutdown or disruption at our manufacturing facility 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.

Table of Contents

Our manufacturing facility and contract manufacturers must undergo inspections by the FDA and/or the EMEA for compliance with cGMP regulations. In the event these facilities do not continue to receive satisfactory cGMP inspections for the manufacture and testing of our products, we may need to fund additional modifications to our manufacturing or testing processes, conduct additional validation studies, or find alternative manufacturing and testing facilities, any of which would result in significant cost to us as well as a significant delay of up to several years in obtaining additional approvals for IPLEX or continuation of the development of our products. In addition, our manufacturing facility and any contract manufacturer we may utilize will be subject to ongoing periodic inspection by the FDA, the EMEA and other foreign agencies for compliance with cGMP regulations and similar foreign standards. We have limited control over contract manufacturers compliance with these regulations and standards.

Product for our clinical studies is currently made at our manufacturing facility and then sent to contract manufacturers for sterile filtration, filling into vials and some analytical testing. Should our manufacturing facility or our contract manufacturers 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 IPLEX or validation of the manufacturing process for IPLEX. This could delay the sale and marketing of IPLEX, our clinical studies and the approval of our MAA, which would delay or otherwise adversely affect revenues. If the damage to any of these facilities is extensive or if our contract manufacturer is unwilling or unable to perform under our agreements, we will need to find alternative facilities. The number of contract manufacturers with the expertise and facilities to manufacture IPLEX 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 contract manufacturers, we would also need to transfer to these new manufacturers and validate the processes and analytical methods necessary for the production and testing of IPLEX. Any of these factors could lead to (1) the delay or suspension of our clinical studies, regulatory submissions, regulatory approvals or commercialization of IPLEX, or (2) higher costs of production, or (3) our failure to effectively commercialize IPLEX or our other drug candidates.

Furthermore, if our manufacturing 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 IPLEX and we would lose potential revenues.

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, preclinical development, clinical development and/or sales and marketing. For example, almost all of our clinical trial work is done in collaboration with academic institutions and we have licensed intellectual property to permit the development, manufacture and commercialization of IPLEX and our drug candidates. Reliance on collaborative relationships poses a number of risks, including the following:

- we may not be able to effectively control whether our corporate partners will devote sufficient resources to our programs or product;
- 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;

Table of Contents

- 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 long-term viability and growth depend on the successful development and commercialization of our products. Pharmaceutical product development is an expensive, high risk, lengthy, complicated, resource intensive process.

Our long-term viability and growth depend on the successful development and commercialization of additional products which lead to revenue and profits. All of our products other than IPLEX are in the research and development stage. Our products must be successfully developed prior to commercialization. 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, preclinical and other research;
- submit for and receive regulatory approval to perform clinical studies;
- design and conduct appropriate preclinical and clinical studies according to good laboratory and good clinical practices;
- 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.

The development program with respect to any given product will take many years and thus delay our ability to generate profits. In addition, potential products that appear promising at early stages of development may fail for a number of reasons, including the possibility that the products may require significant additional testing or turn out to be:

unsafe;

not effective;

too difficult or expensive to develop or 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;

Table of Contents

attract and retain appropriate personnel; and

develop relationships with other companies to perform various development activities that we are unable to perform.

If our products fail in preclinical or clinical studies or if we cannot enroll enough patients to complete our clinical studies, 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 preclinical studies and clinical studies that the product is safe and effective for use in each target indication. In addition, the results from preclinical testing and early clinical studies may not be predictive of results obtained in later clinical studies. There can be no assurance that our clinical studies will demonstrate sufficient safety and effectiveness to obtain regulatory approvals. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in late stage clinical studies even after promising results in early stage development. If our products fail in preclinical or clinical studies, it may have an adverse effect on our business, financial condition and results of operations.

We are currently conducting a Phase III clinical trial of IPLEX in patients with Severe Primary IGFD and plan to include the data from the trial in a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMEA. We must receive approval of these applications before we can market IPLEX in certain countries outside of the United States. We are also planning and conducting clinical studies with INSM-18 and rhIGFBP-3.

The completion rate of these and other clinical studies 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 studies 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 studies to address concerns that the long-term use of IPLEX 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 studies of rhIGF-1, concerns were raised that long-term use of rhIGF-1 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-1, the FDA may require us to conduct broad, long-term clinical studies to address these concerns prior to receiving FDA approval for broad chronic indications such as diabetes. These clinical studies would be expensive and could delay or prevent our commercialization of IPLEX for these broader chronic indications. Adverse results from these studies could prevent our commercialization of IPLEX for broad chronic indications or could jeopardize existing development and approvals in other indications.

Table of Contents

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:

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

We may also need to spend more money than currently expected because we may change our drug development plans, acquire additional drugs or drug 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. Without additional funding, we do not believe that existing cash reserves, including amounts raised in our March 15, 2005 financing, will sufficiently fund our activities through the next twelve months. Our independent registered public accounting firm has indicated that there are material uncertainties which cast significant doubt upon our ability to continue as a going concern. The addition of this going concern disclosure may discourage investors from purchasing our stock.

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 drug 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. A number of factors affect our ability to attract qualified personnel, including our size, our location, our status as a public company and our uncertain prospects. We face intense competition for such personnel and relationships. We cannot assure that we will attract and retain appropriate persons or maintain such relationships.

Table of Contents

We expect that our potential expansion into areas and activities requiring additional expertise, such as further clinical studies, governmental approvals, manufacturing, sales, marketing and distribution will place additional requirements on our management, operational and financial resources. We expect that 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.

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. We currently maintain a general liability insurance policy that has a $1.0 million per claim limit and also caps aggregate claims at $2.0 million. In addition, we have an umbrella insurance policy that covers up to $2.0 million of liability in excess of the general liability policy s $2.0 million limit. In the event of an accident, we could be held liable for damages, which would likely exceed our insurance coverage and other available financial resources. This liability would limit our ability to commercialize IPLEX and develop other products which would 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 studies 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 on our business, financial condition and results of operations.

It is illegal for us to promote IPLEX for uses other than those approved by the regulatory authorities. Such off-label promotion, as it is known, may result in regulatory actions against us even if such activities by us are inadvertent.

Physicians may prescribe drugs for uses that are not described in the product s labeling and that differ from those approved by the FDA. Such off-label uses are common across medical specialties. Although the FDA does not regulate the practice of medicine, the FDA does restrict our communications with respect to off-label use. We cannot promote FDA-approved drugs for off-label uses. A company may engage in truthful, non-misleading, and non-promotional speech concerning its products. For example, while we may inform physicians that we are conducting a clinical trial to evaluate the safety and effectiveness of IPLEX in unapproved uses and encourage those physicians to refer eligible patients to enroll in the clinical trial, we cannot promote the product for unapproved uses. We may also educate physicians about a particular disease state and how that disease is properly diagnosed so that patients who qualify for the clinical trial might be identified, and survey physicians

Table of Contents

who are lawfully prescribing our products or competitors products for off-label uses to monitor patients experiences. We may also, pursuant to FDA policies, respond to unsolicited requests from health care professionals and engage in appropriate scientific exchange of information about unapproved uses. As we have no sales and marketing experience, we have not engaged in these lawful activities with respect to IPLEX in the past. These rules are complex and our sales and marketing employees may not understand the regulations against off-label promotion. We do not yet have policies and procedures in place to regulate the lawful promotion of our marketed products within their labeled indications. While our employees will be trained to follow specific policies and procedures designed to instruct the lawful promotion of our products and must certify that they will abide by them, we cannot guarantee that our employees will follow these policies and procedures. The FDA actively enforces regulations prohibiting promotion of off-label uses and the promotion of products for unapproved uses. The FDA s regulations and policies are subject to varying interpretations, which are evolving. We cannot guarantee that we will change our policies as the FDA s regulations and policies change. Failure to comply with these regulations and policies can result in regulatory enforcement action by the FDA and other governmental bodies, which would have an adverse effect on our revenues, business and financial prospects.

Conversion of our outstanding notes and exercise of warrants and options issued by us will significantly dilute the ownership interest of existing shareholders.

As of February 28, 2006, the convertible notes issued by us on March 15, 2005 and the warrants issued by us in March 2005, November 2004 and July 2003 were convertible into and exercisable for up to approximately 13.2 million shares of our common stock, representing approximately 17% of our then outstanding common stock.

As of February 28, 2006, our outstanding options to our employees, officers, directors and consultants were exercisable for up to 6.1 million shares of our common stock, representing approximately an additional 8% of our then outstanding common stock.

The conversion or exercise of some or all of our convertible notes, warrants and options will significantly dilute the ownership interests of existing shareholders. Any sales in the public market of the common stock issuable upon such conversion or exercise could adversely affect prevailing market prices of our common stock.

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 relate to:

- our listing status on The Nasdaq National Market;
- results of our clinical studies and preclinical studies, or those of our corporate partners or our competitors;
- our operating results;
- developments relating to patent or other litigation in which we are involved;
- 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 announcements of new products,

government regulation, reimbursement changes and governmental investigation or audits related to us or to our products,

developments related to our patents or other proprietary rights or those of our competitors;

Table of Contents

changes in the position of securities analysts with respect to our stock; and/or

operating results below the expectations of public market analysts and investors.

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

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, 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 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 Rights Plan under which shareholders received rights to purchase new shares of preferred stock if a person or group acquires 15% or more

Table of Contents

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.

Our common stock may be thinly traded from time to time, which means large transactions in our common stock may be difficult to conduct in a short time frame.

On occasion, we have a low volume of daily trades in our common stock on The Nasdaq National Market. Any large transactions in our common stock may be difficult to conduct and may cause significant fluctuations in the price of our common stock.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates.

Our long term growth strategy may include 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 eventually 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.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

We believe it is important to communicate our expectations to investors. However, there may be events in the future that we are not able to predict accurately or that we do not fully control that could cause actual results to differ materially from those expressed or implied. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in the accompanying prospectus may contain forward looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such statements are subject to certain factors, risks and uncertainties that may cause actual results, events and performances to differ materially from those referred to in such statements. Statements that are subject to these risks and uncertainties address operating performance, events or developments that we expect or anticipate will occur in the future, such as the commercialization of IPLEX, projections about our ongoing clinical studies, including their costs, projections about our future results of operations or our financial condition, research, development and commercialization of our drug candidates, the potential outcome of any litigation and the effect any litigation might have on our business, financial condition and results of operations, the commercial potential of additional drug candidates or indications for existing drugs, sufficient and timely enrollment of suitable patients in our clinical studies, whether early-stage clinical trial results are any indication of results in subsequent clinical studies, anticipated trends in our business, manufacture of sufficient and acceptable quantities of our current and proposed drugs on a timely and cost efficient basis, approval of our drug candidates, meeting additional capital requirements and other risks that could cause actual results to differ materially. The forward looking statements are based on information available to us on the date hereof, and we assume no obligation to update any such forward looking statements.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from this offering after deducting the underwriting discounts and commissions and estimated offering expenses payable by us will be approximately $44.1 million, ($50.7 if the over-allotment option is exercised in full), assuming a public offering price of $2.37 per share. A $0.25 increase (decrease) in the assumed public offering price of $2.37 per share would increase (decrease) the net proceeds to us from this offering by $4.7 million, or $5.3 million if the over-allotment option is exercised in full, assuming the number of shares offered by us, as set forth on the cover page of this preliminary prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering for working capital and for other general corporate purposes, including the continuing commercial launch of IPLEX, manufacturing IPLEX, pursuit of marketing authorization for IPLEX in Europe and clinical studies.

While we have estimated the particular uses for the net proceeds to be received upon the completion of this offering, we cannot specify these uses with certainty. Our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of our management regarding the application of the proceeds of this offering. Pending these uses, we plan to invest the net proceeds in short-term, interest bearing obligations, investment grade instruments, certificates of deposit or direct or guaranteed obligations of the United States.

PRICE RANGE OF COMMON STOCK

The following table shows for the periods indicated the high and low closing prices for our common stock on The Nasdaq National Market during the periods indicated. Our stock symbol is INSM.

	High	Low
Year Ended December 31, 2004		
First Quarter	$ 4.28	$ 2.87
Second Quarter	$ 3.40	$ 1.98
Third Quarter	$ 2.33	$ 1.00
Fourth Quarter	$ 2.48	$ 1.24
Year Ended December 31, 2005		
First Quarter	$ 2.30	$ 0.80
Second Quarter	$ 1.45	$ 0.79
Third Quarter	$ 1.64	$ 0.86
Fourth Quarter	$ 2.04	$ 1.10
Year Ending December 31, 2006		
First Quarter (through March 3, 2006)	$ 3.35	$ 1.95

On March 3, 2006, the last reported sale price for our common stock on The Nasdaq National Market was $2.37 per share. As of March 3, 2006, there were approximately 585 holders of record of our common stock.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain earnings, if any, to support the development of our business and do not anticipate paying cash dividends for the foreseeable future.

Table of Contents

CAPITALIZATION

The following table sets forth our consolidated capitalization as of December 31, 2005 (1) on an actual basis and (2) on an as adjusted basis to reflect the sale of 20,000,000 shares of our common stock in this offering at an assumed offering price to public of $2.37 per share, after deducting the underwriting discounts and commissions and estimated offering expenses. The information in this table is based upon shares outstanding as of December 31, 2005 and excludes:

- 22,550,332 shares of common stock issuable upon the exercise of stock options and warrants outstanding as of December 31, 2005 and having a weighted average exercise price of $2.03 per share;
- 8,832,432 shares issuable upon the conversion of convertible notes with an aggregate principal amount of $11,438,000 outstanding as of December 31, 2005; and
- 2,736,095 shares available for issuance under our equity incentive plans as of December 31, 2005.

Between January 1, 2006 and February 28, 2006, 4,189,189 shares of common stock were issued upon the conversion of convertible notes with an aggregate principal amount of $5,425,000, and warrants and options were exercised for 6,405,921 shares of common stock. The proceeds payable to the Company on these warrant and option exercises were $8,821,902. None of these 10,595,110 shares issued upon conversion of convertible notes or exercise of warrants and options are included in the number of shares of common stock listed above as outstanding after the offering.

This table should be read in conjunction with the detailed information and financial statements appearing in documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

	As of December 31, 2005	
	Actual	As Adjusted
	(in thousands, except share and per share data)	
Cash and cash equivalents(1)	$ 18,835	$ 62,917
Net Convertible Debt	$ 6,437	$ 6,437
Stockholders equity:		
Common stockholders equity ($0.01 par value, 500,000,000 shares authorized; 66,525,792 shares issued and outstanding, actual; and 86,525,792 shares issued and outstanding, as adjusted)	665	865
Additional Paid-in capital	264,522	308,604
Accumulated deficit	(254,658)	(255,570)
Total Stockholders equity(1)	10,529	54,611
Total capitalization(1)	$ 22,870	$ 66,952

(1) A $0.25 increase (decrease) in the assumed public offering price of $2.37 per share would increase (decrease) each of Cash and Cash Equivalents, Common Stockholders equity, Total Stockholders equity and Total capitalization by $4.7 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Table of Contents

BUSINESS

Our Business

Insmed Incorporated is a biopharmaceutical company focused on the development and commercialization of drugs to treat metabolic diseases and endocrine disorders within niche markets that have unmet medical needs. Currently, our development and commercial activities involve drugs that modulate Insulin-like Growth Factor-1, IGF-1, activity in the human body. Our lead product, IPLEX (mecasermin rinfabate [rDNA origin] injection), is the only FDA approved, once-daily IGF-1 replacement therapy. IPLEX was approved in December 2005 for the treatment of growth failure in children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone (Severe Primary IGFD). As an Orphan Drug, IPLEX is entitled to seven years of marketing exclusivity for IPLEX in the treatment of Severe Primary IGFD in the United States. We are conducting and plan to pursue further clinical trials in order to expand the label for IPLEX into additional clinical indications.

We are building our own specialty sales force to launch IPLEX in the United States in the second quarter of this year. We believe we can effectively market IPLEX by targeting the top 400 pediatric endocrinologists in the United States who we estimate treat the substantial majority of the approximately 6,000 children who suffer from severe short stature due to Severe Primary IGFD. The positive therapeutic characteristics of IPLEX that we believe will make it a commercial success are:

- IPLEX has demonstrated statistically significant increases in linear growth.
- IPLEX is the only once-daily IGF-1 replacement therapy approved for use in the United States.
- IPLEX may be administered either in the morning or evening.
- IPLEX has demonstrated an acceptable safety profile.

We believe the commercial opportunities for IPLEX are significant and reach beyond our approved indication of Severe Primary IGFD. Subject to completion of additional clinical studies and regulatory approval, the initial approval of IPLEX may offer us an opportunity for label expansion into other indications, most with larger patient populations than Severe Primary IGFD. We are currently conducting Phase II clinical studies in patients with myotonic muscular dystrophy, HIV associated adipose redistribution syndrome and extreme insulin resistance. We also intend to conduct additional clinical studies in other growth disorders associated with IGF-1 deficiency.

We also intend to expand the market for IPLEX by pursuing approvals outside of the United States, including the European Union. We have been granted Orphan Drug Designation by the European Medicines Agency for the Evaluation of Medicinal Products, or the EMEA, for IPLEX in the treatment of primary growth hormone insensitivity syndrome (Laron Syndrome) or GHIS. We intend to expand this designation to include Severe Primary IGFD should this approval be granted by the EMEA. Should approval of IPLEX be granted for this indication by the EMEA, as an Orphan Drug, IPLEX will be provided up to 10 years of marketing exclusivity in the European Union. We plan to file for marketing authorization with the EMEA in the third quarter of 2006.

In addition to our IPLEX development and commercialization programs, we have an oncology program focused on two compounds, INSM-18 and rhIGFBP-3. Our longer-term development efforts are primarily focused on the potential to treat cancers by using these compounds to target growth factors and their receptors. Our small molecule compound, INSM-18, has novel effects on the activity of the IGF-1 and other receptors, such as Her2/Neu, and may lead to the inhibition of growth of various tumors. A Phase I/II clinical study of INSM-18 in refractory prostate cancer patients has been initiated at the University of California, San Francisco School of Medicine. rhIGFBP-3 is a naturally occurring anti-tumor agent normally found in the human bloodstream. Several epidemiological studies have demonstrated that cancer risk increases as levels of rhIGFBP-3 in the blood decrease. A Phase I clinical study to evaluate rhIGFBP-3 safety and tolerance in human volunteers is in progress.

Table of Contents

Our Business Strategy

We intend to capitalize on the therapeutic opportunities presented by IPLEX by commercializing it in its approved indication in the United States and extending the use of IPLEX in other indications and other geographic markets. We also intend to develop, seek regulatory approval of and commercialize other drugs for the treatment of other metabolic diseases and endocrine disorders with unmet medical needs. This includes the development of cancer treatments based on our expertise in IGF-1 biology. Both the INSM-18 and rhIGFBP-3 development programs are based on the belief that these product candidates modulate the over expression of IGF-1 and its receptors in solid tumors. Key elements of our strategy include:

Launch IPLEX commercially in 2006 with our own specialty sales force. We are building a sales and marketing force to target approximately 400 U.S.-based pediatric endocrinologists who we estimate treat the substantial majority of the children with Severe Primary IGFD. These physicians are readily accessible because they are primarily hospital-based and located in major metropolitan areas. We have hired a management team for our sales, marketing, medical communications and managed care groups that will bring IPLEX to the market. By the end of 2006, we expect to employ 25 to 30 sales representatives. In addition, we intend to conduct continuing medical education programs, medical symposia, and regional speaker programs aimed at establishing awareness of IPLEX in the medical community.

Develop IPLEX in additional non-growth disorder indications. We intend to initiate clinical studies of IPLEX in the United States in additional indications where existing preclinical or clinical data suggest IPLEX may be an effective treatment. We have initiated studies in myotonic muscular dystrophy (estimated U.S. patient population is 40,000), HIV associated adipose redistribution syndrome (estimated U.S. patient population is at least 80,000) and extreme insulin resistance.

Expand the Severe Primary IGFD indication to other growth disorders related to IGF-1 deficiency. There are a number of growth disorders related to IGF-1 deficiency other than Severe Primary IGFD which represent conditions with significant unmet medical needs and significant opportunities for expansion of the market for IPLEX. We plan to investigate these other indications and further develop those that provide the best market opportunity for label expansion. We believe that successful label expansion studies in IGF-1-related short stature may expand the U.S. market for IPLEX from 6,000 children to approximately 35,000 children. We intend to initiate a Phase II study in children with Noonan Syndrome, a population with IGF-1 deficiency, in the second quarter of this year.

Establish a commercialization strategy for IPLEX outside the United States. We will either build our own European sales and marketing team or explore opportunities to partner with an established sales and marketing organization in Europe. We intend to file a Marketing Authorization Application, or MAA, with the EMEA for approval of IPLEX in the European Union for the treatment of an indication that is very similar to the indication for which we recently received approval from the FDA in the United States. We also intend to seek regulatory marketing authorization of IPLEX in additional territories, including Israel and certain Middle Eastern states and South America.

Develop Oncology Portfolio. We will continue to conduct clinical studies of INSM-18 and rhIGFBP-3 for the treatment of cancer. Based on the results of these studies, we will evaluate opportunities to initiate Phase II clinical studies in one or more of the following cancer types: breast, colorectal, lung or prostate. We will either conduct additional studies independently or enter into development or licensing agreements with companies with greater expertise in the development of cancer therapies.

Table of Contents

Product Pipeline

Name	Indication	Status
IPLEX	Growth Failure associated with Severe Primary IGFD	FDA Approved
IPLEX	Myotonic Muscular Dystrophy	Phase II
IPLEX	HIV Associated Adipose Redistribution Syndrome (HARS)	Phase II
IPLEX	Extreme Insulin Resistance	Phase II
IPLEX	Growth Failure associated with IGF-1 Deficiency (Noonan Syndrome)	Phase II Planned
INSM-18	Refractory Prostate Cancer	Phase I/II
rhIGFBP-3	Cancer	Phase I

IPLEX

IPLEX is our proprietary drug for the delivery of recombinant insulin-like growth factor 1 (IGF-1). It is administered as a preformed complex with a recombinant form of its natural binding protein, insulin-like growth factor binding protein 3 (rhIGFBP-3). This novel compound is administered as a once-daily subcutaneous injection, which can restore and maintain IGF-1 levels to physiologically relevant levels. The binding protein, rhIGFBP-3, extends the residence time of IGF-1 in the blood, mimicking normal human physiology. In the bound state, we believe IGF-1 is inactive, and remains so until delivered to target tissues in the body where it is released and becomes biologically active.

IPLEX s Approved Indication

Growth Failure Due to Severe Primary IGFD. Severe primary IGF-1 deficiency or Severe Primary IGFD is a condition which causes growth failure and extreme short stature due to a marked deficiency in IGF-1. This deficiency can be due to hereditary defects in the growth hormone receptor or post-receptor pathway, or due to acquired causes such as growth hormone antibodies in patients with growth hormone gene deletion. Characteristics of this condition can include:

- normal or elevated serum growth hormone levels;
- inability to generate normal IGF-1 levels after growth hormone provocation;
- reduced serum IGF-1 and rhIGFBP-3 levels;
- severe postnatal growth failure and markedly reduced adult height;
- truncal adiposity; and
- delayed skeletal maturation.

Physicians characterize a child s height deficit by calculating a height standard deviation score, or height SDS, which indicates how many standard deviations a child s height is from the average value for 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 Primary IGFD have a height SDS that is at least three standard deviations below the average. Children with Severe Primary IGFD who are untreated will typically attain a final height of no more than approximately 5 1 (155 cm) for boys and 4 9 (146 cm) for girls. Historically, prior to the approval of an IGF-1 therapy, the only treatment for severe short stature has been human growth hormone

(hGH). However, it has been long recognized that there are a significant group of children who do not adequately respond to hGH due to growth hormone insensitivity.

Table of Contents

Approximately 380,000 children in the United States are referred each year to pediatric endocrinologists for evaluation of possible short stature. We believe approximately 6,000 of these children suffer from Severe Primary IGFD and may be treated with IPLEX.

We are preparing to commercially launch IPLEX with our own sales force in the United States in the second quarter of 2006. In addition, we are currently assessing our regulatory strategy regarding submission of a Marketing Authorization Application, with the European Medicines Evaluation Agency for IPLEX treatment of Severe Primary IGFD. We intend to file our MAA in Europe by the end of the third quarter of 2006.

Ongoing Clinical Trial

We have results from an ongoing Phase III study of 47 children with Severe Primary IGFD. Twenty-six of these 47 children completed at least 6 months of IPLEX replacement therapy and were evaluable for efficacy at 6 months, which is the generally accepted minimum length of time required to adequately measure growth response to drug therapy. A statistically significant increase in average growth rate from 3.4 cm per year prior to treatment to 7.4 cm per year during the first 6 months of IPLEX treatment was demonstrated in the lower dose group, where as the increase was from 2.2 cm per year to 8.8 cm per year in the higher dose group ($p<0.0001$ for both groups). A p-value of less than 0.0001 means that the probability that this result occurred by chance was less than 1 in 10,000. A probability of 5 in 100 or less, or $p<0.05$, is commonly considered to be statistically significant. With this six-month data, IPLEX was approved for marketing by the FDA on December 12, 2005.

Twenty-four of the subjects have received at least 12 months of treatment and qualified for inclusion in the 12 month analysis. These subjects experienced a statistically significant increase in growth rate from 3.4 to 6.4 cm/year and 2.0 to 8.3 cm/year over the 12 month treatment period in the low and high dose groups, respectively ($p<0.0001$ for both groups). Although three patients left the study before completion, none of the 47 patients discontinued IPLEX treatment due to adverse events considered related to drug. Some patients experienced hypoglycemia, or low blood glucose levels. Enlargement of the tonsils and headaches were also noted in some patients.

We believe that increases in growth rates resulting from IPLEX treatment were clinically meaningful, leading to catch-up growth as indicated by a significant increase in height SDS. These results are comparable to those observed in clinical studies of other approved growth indications for other growth-promoting therapies.

Other Indications for IPLEX in Development

Myotonic Muscular Dystrophy. Myotonic muscular dystrophy or MMD (also known as myotonic dystrophy, dystrophia myotonica or Steinert s disease) is the most common type of adult muscular dystrophy and affects approximately 1 in 8,000 individuals. MMD causes progressive muscle wasting and weakness in the hands, forearms, legs, neck and face. It often involves many other systemic effects, including endocrine abnormalities, especially with respect to insulin, a regulator of blood sugar (glucose); neurological changes, including excessive sleepiness and apathy; cataracts, usually requiring surgical excision; gastrointestinal problems; and cardiac rhythm abnormalities, often requiring pacemaker insertion. In extreme cases, these patients can eventually become totally disabled, dying usually from respiratory or cardiac failure. At present, there is no treatment to reverse most of these symptoms. Previous preclinical and human studies have demonstrated that IGF-1 therapy may be an effective treatment for myotonic muscular dystrophy.

Based on information published by the Muscular Dystrophy Association, we believe that there are approximately 40,000 patients that suffer from MMD in the United States.

Ongoing Clinical Study

A Phase II clinical study program investigating IPLEX as a treatment for MMD has been initiated by the University of Rochester School of Medicine, with funding provided by the Muscular Dystrophy Association and

the National Institute of Health. This Phase II program is designed to investigate the safety and tolerability of once-daily subcutaneous injections of IPLEX in patients with MMD using two sequential studies each involving 15 patients. The first study is a 24-week, dose-escalation study of IPLEX intended to identify an optimal dose for the subsequent 24-week, fixed-dose study. Both studies will evaluate a number of safety parameters in a prospective manner, as well as several key efficacy measures such as muscle mass and strength.

The University of Rochester has been designated by the National Institutes of Health (NIH) as one of several centers of excellence for muscular dystrophy research. As such, the University of Rochester is eligible to receive funding from the NIH and Muscular Dystrophy Association. A portion of this funding is being used to substantially fund this clinical study.

HIV Associated Adipose Redistribution Syndrome (HARS). HIV-associated adipose redistribution syndrome, or HARS, is characterized by fat maldistribution in HIV-infected patients. Patients with HARS experience abnormal, pathological accumulation of adipose tissue in the trunk, primarily in the form of visceral adipose tissue located deep within the abdomen, underneath the abdominal muscle wall. This fat accumulation may be present with or without fat depletion, lipoatrophy, and/or metabolic abnormalities. In general, HARS patients accumulate excess visceral adipose tissue in the abdomen or may develop a fat pad on the upper back commonly known as a buffalo hump. This condition is sometimes referred to as HIV Lipodystrophy.

Since the advent of highly active antiretroviral therapy, or HAART, there has been a marked increase in adverse metabolic effects in HIV patients on antiretroviral treatments. These adverse effects include insulin resistance, hyperglycemia, dyslipidemia and changes in body fat distribution that include syndromes of both central fat accumulation (visceral adiposity and buffalo hump) and fat loss in the limbs. Recent studies performed in subjects on HAART suggest that at least 20% of individuals develop the morphologic features of this syndrome. With the similarity of HARS to metabolic syndrome X, which has been associated with increased risk of cardiovascular disease, it is now feared that these HAART side effects may impact the long-term prognosis in patients whose life expectancies have been significantly extended due to effective viral suppression by HAART. At present, there is no approved treatment for this condition.

We believe that there are at least 80,000 patients who suffer from HARS in the United States.

Ongoing Clinical Study

A Phase II clinical study investigating IPLEX as a treatment for HARS has been initiated by the University of California, San Francisco. This Phase II open-label study is designed to evaluate the safety and efficacy of 12 weeks of IPLEX treatment in 12 subjects with HARS. To qualify for inclusion in the study, patients must be between 18-65 years of age, have confirmed HIV-1 infection and fat accumulation (visceral adiposity). The primary goal of the study is to determine the effects of IPLEX on visceral fat and glucose and lipid metabolism.

Extreme Insulin Resistance. Syndromes of extreme insulin resistance result from genetic defects in the insulin receptor or insulin signaling pathways and include Type A and Type B Syndromes, Rabson-Mendenhall Syndrome and Leprechaunism. In addition to insulin resistance and glucose intolerance or overt diabetes, these syndromes share a number of common features, including variable degrees of hyperandrogenism, hirsutism, and dysmorphic features. Individuals with extreme insulin resistance who develop frank diabetes require large doses (>200 units/day) of subcutaneous insulin, oral hypoglycemic agents and insulin sensitizers. Despite this intense regimen, glycemic control remains poor and these patients are at high risk of the complications of diabetes such as cardiovascular disease, nephropathy, retinopathy and neuropathy. Previous Phase II clinical studies completed with IPLEX in diabetic patients have shown improved glycemic control, improved insulin sensitivity as well as a reduction in daily insulin consumption. IPLEX has been granted Orphan Drug Designation in both the United States and Europe for extreme insulin resistance.

Table of Contents

Ongoing Clinical Study

We have initiated a Phase II clinical study at the University of Cambridge to investigate the therapeutic benefit of treating Type A and Rabson-Mendenhall Syndrome extreme insulin resistance with IPLEX. This Phase II, open-label, dose-ranging study is designed to evaluate the safety and efficacy of 16 weeks of IPLEX treatment in 10 patients with Type A extreme insulin resistance or Rabson-Mendenhall Syndrome. To qualify for inclusion in the study, patients must be between 10-65 years of age and have a diagnosis of Type A extreme insulin resistance or Rabson-Mendenhall Syndrome. The primary efficacy endpoints of the trial are improvement in glycemic control, improvement in insulin sensitivity, reduction in hemoglobin A1c and improvement in body composition. We expect to present interim data at Endocrine Society s Annual Meeting in June 2006 (ENDO 2006), and complete the trial by the end of 2006.

Noonan Syndrome. Noonan Syndrome is a congenital disorder characterized by a deficiency in IGF-1, short stature, heart defects and variable dysmorphic features. Growth failure is a consistent feature of Noonan Syndrome and the response to recombinant human growth hormone therapy has been disappointing, particularly in children with an identified gene mutation.

With an incidence of approximately one in 2,000, we estimate that there are approximately 30,000 children in the United States with Noonan Syndrome.

Planned Clinical Study

We plan to conduct a Phase II, open-label, multicenter, clinical study to evaluate the pharmacokinetics, safety and efficacy of 12 months of IPLEX treatment in 24 children with growth failure due to Noonan Syndrome. The IPLEX dose will be titrated to maintain IGF-I SDS in the upper normal range. The primary and secondary efficacy measures are annualized height velocity and height SDS, respectively.

Long-Term Development Opportunity for IPLEX

Diabetes. As an extension of studies related to extreme insulin resistance and as one of our longer-term development initiatives, we believe that IPLEX may have application in the treatment of diabetes.

Data from several Phase II studies conducted with IPLEX indicate that IPLEX has a beneficial effect in lowering glucose levels, and insulin demands. 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 growth hormone receptors in the liver results in reduced circulating IGF-1 levels, which can lead to growth hormone hypersecretion. This, in turn, causes decreased insulin sensitivity and worsening of metabolic control. We believe treatment of type 1 diabetes with IPLEX may reduce growth hormone 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-1, these patients have an increased number of insulin/IGF-1 hybrid receptors. Increased expression of these hybrid receptors positively correlates with a decrease in both insulin binding affinity and insulin sensitivity. We believe treatment of type 2 diabetics requiring insulin therapy with IPLEX may lead to improved glycemic control while decreasing the insulin dose requirement.

According to the ADA, approximately 73% of insulin-using type 2 diabetes patients are not adequately controlling their blood sugar levels to the ADA recommended guidelines. We believe that there are approximately one million insulin-using diabetes patients who do not adequately control their blood sugar. Since clinical studies for this indication are likely to be very large and expensive, we have no current plans to pursue a clinical development program on our own, however, we may look for a partner to assist us with this clinical development program.

Table of Contents

Oncology Programs INSM-18 and rhIGFBP-3

INSM-18 and rhIGFBP-3 are in early clinical development and are primarily being investigated for the treatment of cancer. 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 alternatives to existing treatments which generally include cytotoxic agents that significantly decrease patient quality of life. To this end, we believe both INSM-18 and rhIGFBP-3, are promising potential novel treatments for a variety of cancer types. Preclinical models demonstrate that both treatments interact with the IGF system to reduce tumor growth.

INSM-18

INSM-18 is an orally available small molecule tyrosine kinase inhibitor that has demonstrated selective inhibition of IGF-1 and human epidermal growth factor receptor (Her2/Neu). It has demonstrated anti-tumor activity in preclinical studies of breast, lung, pancreatic and prostate tumors. Two single dose Phase I clinical studies have been previously completed with INSM-18. In both studies, INSM-18 was safe and well tolerated.

The American Cancer Society estimated that 232,000 new cases of prostate cancer occurred in the United States in 2005. It was also estimated by the American Cancer Society that 30,350 deaths occurred as a result of prostate cancer, making it the second leading cause of cancer death in men.

Ongoing Clinical Study

The University of California, San Francisco, has initiated a dose-escalating Phase I/II clinical study designed to define the maximum tolerated dose of INSM-18 in patients with relapsed prostate cancer. The study will consist of a 28-day extension at each dose level to investigate the effect of INSM-18 on prostate-specific antigen levels.

rhIGFBP-3

Although IGF-1 is critical for normal growth and metabolism, aberrant signaling through this pathway is closely linked to the abnormal and unregulated growth of a variety of tumors. Blocking tumor-associated IGF signaling has been proven to prevent tumor growth in a variety of preclinical models. rhIGFBP-3 has demonstrated preclinical efficacy in numerous cancer indications, including breast, prostate, liver, ovarian, and colon cancers. Additionally, several lines of recent evidence from various cell systems have suggested that rhIGFBP-3 may play a more active, IGF-1-independent role in growth regulation of cancer cells, binding specifically with high affinity to the surface of various cell types and directly inhibiting monolayer growth of these cells in an IGF-1-independent manner. Recent independent studies have demonstrated that when IGFBP-3 is used in combination it can accentuate and even synergize the efficacy of standard cancer therapies. Paclitaxel-induced apoptosis is accentuated by rhIGFBP-3, which has been shown to sensitize cells to apoptotic signals such as irradiation and ceramides. Preclinical in vitro and in vivo studies performed by us corroborate previously published reports regarding rhIGFBP-3 s efficacy when administered alone or in combination therapy.

Ongoing Clinical Trial

We have initiated a Phase I clinical study with rhIGFBP-3. The Phase I clinical study is an open-label, dose-escalation study designed to evaluate the safety, tolerability and pharmacokinetics of a single intravenous dose of rhIGFBP-3. The primary goal of this 30-patient study is to identify the appropriate dose of rhIGFBP-3 for a planned Phase II clinical trial in breast cancer.

Research and Development

We have devoted substantially all of our resources since we began our operations to the research and development of a number of drug candidates for metabolic and endocrine diseases. Our research and development efforts are now principally focused on conducting additional clinical studies, further developing our

Table of Contents

approved drug, IPLEX, and expanding the label for IPLEX into other indications. We conduct very little of our own preclinical laboratory research. We are currently conducting a worldwide Phase III clinical study with our lead drug, IPLEX, and we are also conducting clinical studies with our anti-cancer drug candidates, INSM-18 and rhIGFBP-3 and plan on conducting additional clinical studies with these drugs in the future.

Research and development expenses primarily include expenses incurred in preparing and obtaining the approval from regulatory bodies, certain expenses involving the development of manufacturing processes and clinical studies (including necessary quantities of drugs being studied). Our research and development expenses were approximately $23.3 million in 2004 and $21.8 million for the year ended December 31, 2005. The amount spent on research and development relative to the overall budget is expected to decrease now that we are dedicating a greater proportion of our resources to the commercialization of IPLEX.

Manufacturing

We currently manufacture our own supply of bulk IPLEX and rhIGFBP-3 at our FDA approved facility in Boulder, Colorado. The manufacturing process requires compliance with current good manufacturing practices, or cGMP, and other similar regulations. IPLEX is a complex of two proteins, rhIGF-1 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-1 and rhIGFBP-3 are produced separately and then combined to make IPLEX. The rhIGFBP-3 can either be utilized to make IPLEX or kept separate as its own distinct product. We currently outsource to third party contract manufacturers some of the analytical testing and the final fill, finish and labeling of IPLEX.

As part of ongoing regulatory compliance, it is likely that the FDA will inspect our manufacturing facilities and our contract manufacturers facilities from time to time to ensure compliance with cGMP. If these facilities are not in compliance with cGMP, the FDA will likely require us to halt manufacturing until we bring the facilities into compliance. This could take a substantial period of time and could adversely affect the development and timing of our clinical studies and/or commercial sales of IPLEX. If for any other reason we are unable manufacture sufficient quantities of our drug candidates and their components which meet our planned time and cost parameters, the commercialization of IPLEX and the development and timing of our clinical studies for additional indications may be adversely affected.

We expect to expend significant resources for the expansion and modification of our manufacturing facility over the next three years in an effort to increase our production capacity and the efficiency of our operations. We believe this facility will meet our commercial and clinical needs for at least the next three years.

Marketing and Sales

Our sales and marketing efforts will initially target the sale of IPLEX to patients being treated by the approximately 400 U.S.-based pediatric endocrinologists who we estimate treat the substantial majority of children with Severe Primary IGFD. 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 IPLEX 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 IPLEX.

The marketing and selling of IPLEX will be accomplished with an initial group of approximately 25-30 sales professionals with supporting staff in marketing, medical communications and managed care. In total, we expect the commercial operations group will grow to 40-45 people by the end of 2006. Future expansion will largely be driven by the availability of new clinical data and FDA action on future marketing label expansion applications for IPLEX and our other leading drug candidates.

Table of Contents

It is our belief that we can serve the top prescribing pediatric endocrinologists with a focused sales and marketing effort. We plan to launch IPLEX in the second quarter of this year and begin generating prescriptions for treating Severe Primary IGFD at that time. We will distribute IPLEX through an established specialty distributor. Like other high value protein therapeutics, revenues for IPLEX will be recorded with the initiation of each individual prescription. We believe this should allow the company to establish a long-term revenue stream as each patient is expected to remain on IPLEX for an average of 6-10 years. We are currently determining the pricing of IPLEX but anticipate pricing IPLEX within the range of the other currently marketed growth promoting agents.

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 drug candidates for certain niche markets and find commercial partners to develop and market our drugs in markets outside of our current focus.

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 drugs 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.

We hold 28 United States patents relating to the composition, production, antibodies and methods of use for IPLEX and rhIGFBP-3, including:

- Two issued patents for rhIGFBP-3 composition-of-matter;
- 15 therapeutic use patents for IPLEX, IGF-1, 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 IPLEX and pharmaceutical compositions of IPLEX.

As part of the ongoing development of IPLEX, INSM-18 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 IPLEX 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, we recently decided to withdraw one of our patents, EP 451,194, or 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, we have 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.

Table of Contents

As part of our business strategy, we plan to license intellectual property which we feel may be important to the development and commercialization of our products. In April 2005, we were granted a non-exclusive license to certain proprietary manufacturing technology from Avecia Limited. In January 2004, we were granted a non-exclusive license to patent rights pertaining to the use of IGF-1 therapy for the treatment of extreme or severe insulin resistant diabetes from Fujisawa Pharmaceutical Co., Ltd. In November 1998, we were granted a non-exclusive license to certain proprietary manufacturing technology from Brookhaven Science Associates, LLC.

Reflecting our commitment to safeguarding proprietary information, we require our employees and consultants to sign confidentiality agreements. These agreements prohibit unauthorized disclosure of our proprietary information. Despite our efforts to protect our proprietary information, unauthorized parties may attempt to obtain and use our proprietary information. Policing unauthorized use of our proprietary information is difficult and the steps we have taken might not prevent misappropriation, particularly in foreign countries where the laws may not protect our proprietary rights as fully as do the laws of the United States.

We note that there has been increasing litigation in the biopharmaceutical industry with respect to the manufacture and sale of new therapeutic compounds. 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 drugs, such as IPLEX 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.

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 resulting 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.

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 additional potential litigation is likely to 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. hold United States and/or foreign patents possibly directed to the composition, production and/or use of rhIGF-1, rhIGFBP-3, rhIGF-1/rhIGFBP-3 (IPLEX) and/or recombinant proteins. 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. Furthermore, Genentech owns U.S. and foreign patents directed to using IGF-1 to increase the growth rate of certain patients with non-growth hormone-deficient short stature and patients having partial growth hormone insensitivity syndrome.

We can provide no assurance that third parties will not assert additional infringement actions against us. Likewise, we cannot predict with certainty the outcome of such a proceeding. In the event of a successful claim against us for infringement or misappropriation of a third party s proprietary rights, we may be required to:

- pay damages, including up to treble damages and the other party s attorneys fees, which may be substantial;
- cease the development, manufacture, marketing and sale of products that infringe the proprietary rights of others;

Table of Contents

expend significant resources to redesign our product so that it does not infringe the proprietary rights of others, or to develop or acquire non-infringing proprietary rights, which may not be possible and would require additional clinical trials and regulatory approvals;

redesign our product to avoid infringing on third party proprietary rights, which may result in significant regulatory delays associated with conducting additional clinical trials or other steps to obtain regulatory approval; and

obtain one or more licenses from third parties for the infringed proprietary rights, which may not be available to us on acceptable terms or at all.

Furthermore, litigation with any third party, even if the allegations are without merit, would likely be expensive and time-consuming and divert management s attention.

Any conclusions we may have reached regarding non-infringement and invalidity are based in part on a review of publicly available databases and other information. There may be information not available to or otherwise not reviewed by us that might change our conclusions. Moreover, the scope and validity of patent claims are determined based on many facts and circumstances, and in a litigation a court may reach a different conclusion on any given patent claim than the conclusions that we have reached.

We are currently defending infringement claims brought against us. On December 20, 2004, Tercica and Genentech filed a complaint against Avecia Limited and us in the United Kingdom at the High Court of Justice, Chancery Division, Patents Court alleging infringement of EP patent No. 571,417, or the 417 patent. The 417 patent has claims directed to particular uses of a combination of IGFBP-3 and IGF-1. In the complaint, Tercica 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. In May 2005, we filed for summary judgment to dismiss the complaint. Our motion for summary judgment was denied and a trial date in this litigation has not been set.

In addition, on December 23, 2004, Genentech and Tercica sued us for infringement of U.S. Patent Nos. 5,187,151 and 6,331,414 in the United States District Court for the Northern District of California. These patents are directed to certain methods of using IGF-1/IGFBP-3 and methods of producing human IGF-1, respectively. On February 16, 2005, Tercica filed an amended complaint, adding an infringement allegation against us with respect to U.S. Patent No. 5,528,287, or 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. Genentech and Tercica claim that the production or use of IPLEX, a complex of rhIGF-1/rhIGFBP-3, will infringe these patents. We moved to dismiss the amended complaint for lack of jurisdiction and on other grounds. At a hearing on the motion on April 15, 2005, the court granted our motion and dismissed the case with leave for plaintiffs to refile the complaint. A second amended complaint was filed on April 22, 2005 by Genentech and Tercica against us. Among other things, this amended complaint added Celtrix Pharmaceuticals, our wholly-owned subsidiary, as a defendant. We moved to dismiss the portion of the second amended complaint that relates to the 287 patent. On June 29, 2005, the Court denied our motion to dismiss. On July 14, 2005, we filed its answer and counterclaims. In the answer and counterclaims, we denied infringement and sought a declaratory judgment that the asserted patents are not infringed, are invalid, and/or are unenforceable. The reply to the counterclaims by Genentech and Tercica was filed on August 5, 2005. On October 17, 2005, Tercica and Genentech filed a third amended complaint adding Insmed Therapeutic Proteins, our wholly-owned subsidiary, as a defendant. The answer and counterclaims in response to the third amended complaint were filed by us on October 27, 2005. Briefing on patent claim construction issues and summary judgment motions is set to be completed by May 5, 2006, with a claim construction hearing scheduled for May 19, 2006. Discovery is ongoing and a trial date is scheduled for November 2006.

On May 27, 2005, Genentech and Tercica filed a motion for preliminary injunction seeking an order barring us, until trial, from making, using or selling the drug called SomatoKine, (now known as IPLEX) with respect

Table of Contents

to its allegations of infringement of U.S. Patent Nos. 6,331,414 and 5,187,151, and requesting that we be required to share any Orphan Drug Exclusivity it obtains with Tercica. We filed an opposition to the motion for a Preliminary Injunction on June 10, 2005. On June 16, 2005, Genentech and Tercica withdrew their motion for a preliminary injunction, but reserved the right to refile the motion for a preliminary injunction.

We cannot predict with certainty the outcome of proceedings involving Tercica and Genentech. The claim construction ruling and summary judgment rulings to be issued by the court could have an adverse impact on our position in this proceeding, including by narrowing or limiting our defenses. An adverse ruling after trial on any of the claims alleged would have a material adverse effect on 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 drugs, 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 drugs, or alternatively, require us and/or our licensees to cease using such drugs 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 drugs candidates 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 drugs. 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 drugs may materially adversely impact our business, financial condition and results of operations.

Competition

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

We cannot predict the relative competitive position of our drug candidates 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.

Competition for IPLEX

Currently, we are aware of at least one other company, Tercica, that is selling a drug that competes directly with IPLEX. Tercica received approval from the FDA in August 2005 for its twice-daily IGF-1 injection drug, Increlex , for the long-term treatment of growth failure in children with Severe Primary IGFD or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone. This indication is substantially similar to the indication for which the FDA approved IPLEX. It is likely that Tercica is planning to develop rhIGF-1 for some of the same indications that we plan to pursue with IPLEX. We are currently engaged in litigation with Tercica related to patent infringement, deceptive promotional statements and unfair business practices claims that Tercica has brought against us.

Table of Contents

We believe that IPLEX has the following positive therapeutic attributes:

- IPLEX has demonstrated statistically significant increases in linear growth.
- IPLEX is the only once-daily IGF-1 replacement approved for use in the United States.
- IPLEX may be administered either in the morning or evening.
- IPLEX has demonstrated an acceptable safety profile.

Growth hormone may also be a competitive product for the treatment of some indications that we may pursue with IPLEX, such as HIV associated adipose redistribution syndrome. 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 studies for the use of its growth hormone in pediatric IGF-1 deficiency. We are also aware that Serono is seeking regulatory approval for its growth hormone, Serostim , for the treatment of HIV associated adipose redistribution syndrome, and that Theratechnologies is conducting Phase III studies for a growth hormone releasing agonist 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 preclinical 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 IPLEX.

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 injectable insulin, inhalable insulin, GLP-1 analogues and oral hypoglycemic drugs.

Further, 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 studies for three products, Symlin, Byetta, and a long-acting release formulation of Byetta, for the treatment of type 2 diabetes. Symlin and Byetta were recently approved for use by the FDA. Tercica has indicated that it plans to pursue the development of rhIGF-1 in the treatment of severe forms of diabetes.

Competition for Our Other Drug Candidates

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 IGF-1 pathway targeted by INSM-18 and rhIGFBP-3. These companies include ImClone, Amgen, OSI Pharmaceuticals, Bristol-Myers Squibb and Genentech.

It is possible that there are other companies with products currently in development or that exist on the market that may compete directly with IPLEX, INSM-18 and rhIGFBP-3.

Deceptive Promotional Statements and Unfair Business Practice Litigation

On December 6, 2005, Tercica filed a complaint against us in the United States District Court for the Northern District of California alleging we made deceptive promotional statements and engaged in unfair

Table of Contents

business practices related to Tercica s product, Increlex, allegedly in violation of the California Business and Professions Code and the Federal Lanham Act. Tercica amended the complaint on December 15, 2005. Tercica is requesting injunctive and monetary relief.

Although we deny any liability, no assurances can be given as to the outcome of this action. An unfavorable settlement or decision could affect 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. Any liability resulting from this action may exceed our financial resources. We have requested that the court dismiss the action on a number of bases, including that Tercica failed to state a claim under the Federal Lanham Act and the court lacks personal jurisdiction over us. We plan to seek attorneys fees from Tercica if the case is successfully concluded.

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. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our products, and we may be criminally prosecuted.

We and our third party manufacturers may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act and import, export and customs regulations.

FDA Approval Process

The steps ordinarily required before a new drug may be marketed in the United States are similar to steps required in many other countries. The process required by the FDA before a new drug may be marketed in the United States generally involves the following: completion of preclinical laboratory and animal testing in compliance with FDA regulations, submission of an Investigational New Drug Application, or IND, which must become effective before human clinical studies may begin, performance of adequate and well-controlled human clinical studies to establish the safety and efficacy of the proposed drug for its intended use, and submission and approval of a New Drug Application, or NDA, by the FDA.

Preclinical tests include laboratory evaluation of product chemistry and stability, as well as animal studies to evaluate toxicity before a drug is administered to human subjects. The results of preclinical testing are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission 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 order the partial, temporary or permanent discontinuation of a clinical trial or impose other sanctions if the FDA believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. Clinical studies must be conducted in accordance with the FDA s good clinical practices requirements. The IND process may become extremely costly and substantially delay development of our products. Moreover, positive results of preclinical tests will not necessarily indicate positive results in clinical studies.

Clinical studies to support NDA approval are typically conducted in three sequential phases, but the phases may overlap. In Phase I clinical studies, the product is tested in a small number of patients or healthy volunteers, primarily for safety at one or more doses and to assess pharmacokinetics. In Phase II clinical studies, in addition to safety, the sponsor evaluates the efficacy of the product on targeted indications, identifies possible adverse effects and safety risks in a patient population, and assesses dose tolerance and optimal dose range. If a compound is found to be potentially effective and to have an acceptable safety profile in Phase II studies, Phase III studies, also referred to as pivotal studies, are undertaken. Phase III clinical studies typically involve testing for safety and clinical efficacy in an expanded patient population at geographically-dispersed study sites.

Table of Contents

After completion of the required clinical testing, an NDA is submitted. An NDA contains the results of the preclinical and clinical studies, together with, among other things, detailed information on the manufacture and composition of the product and proposed labeling, including payment of a user fee. The FDA may request additional information before accepting an NDA for filing, in which case the application must be resubmitted with the additional information. During its review of an NDA, the FDA may refer the application to an appropriate advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee.

Under the policies agreed to by the FDA under the Prescription Drug User Fee Act, or the PDUFA. Once the NDA is accepted for filing by the FDA, the FDA has 10 months in which to complete its initial review of a standard NDA and respond to the applicant, and 6 months to initially review and respond to a priority NDA. Standard NDA status or priority NDA status are based on several factors identified by the FDA including for example, whether the drug product, if approved, would be a significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease. The review process and the PDUFA goal date may be extended by 3 months if the FDA requests, or the NDA sponsor otherwise submits, a major amendment containing additional information or clarification regarding information already provided in the submission within the last 3 months of the PDUFA goal date.

If the FDA s evaluation of the NDA, and the FDA inspections of the clinical investigators and the facilities are favorable, the FDA may issue either an approval letter or an approvable letter. An approvable letter contains the conditions that must be met in order to secure approval of the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will issue an approval letter. An approval letter authorizes commercial marketing of the drug for certain approved indications. In addition, an approval letter may contain various post-marketing commitments or agreements, which are often referred to as Phase IV studies. If the FDA s evaluation of the NDA submission, clinical investigation or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA and issue a not approvable letter.

The manufacturers of approved products and their manufacturing facilities are subject to continual review and periodic inspections. Because we may contract with third parties for manufacturing of our products, our ability to control compliance with FDA requirements may be incomplete. In addition, after any of our drugs are on the market, identification of certain side effects or the occurrence of manufacturing problems could cause product recall, withdrawal of approval, reformulation of the drug, additional preclinical testing or clinical studies, or labeling changes.

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

The Hatch-Waxman Act

The Drug Price Competition and Patent Term Restoration Act of 1984 or Hatch-Waxman Act amended the Federal Food, Drug, and Cosmetic Act. Under the Hatch-Waxman Act, newly-approved drugs and indications may benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act provides 5-year marketing exclusivity to the first applicant to gain approval of an NDA for a new chemical entity, meaning that the FDA has not previously approved any other new drug containing the same active moiety. However, in the case of a combination drug containing a new chemical entity and a non-new chemical entity, 5-year exclusivity does not attach to the new chemical entity. The Hatch-Waxman Act prohibits the submission of an Abbreviated NDA, or ANDA, for a generic drug, or a Section 505(b)(2) NDA for another version of such drug during the 5-year exclusive period. However, the submission of an ANDA or Section 505(b)(2) NDA containing a paragraph IV certification claiming that a patent listed in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, or Orange Book for the drug is invalid or will not be infringed by the manufacture, use or sale of the new product is permitted after four years. The submission of a paragraph IV certification may trigger a 30-month stay of approval of the ANDA or Section 505(b)(2) NDA. Protection under

Hatch-Waxman will not prevent the submission or approval of another full NDA; however, the applicant would be required to conduct its own preclinical and adequate and well-controlled clinical studies to demonstrate safety and effectiveness. The Hatch-Waxman Act also provides 3 years of marketing exclusivity for the approval of new and supplemental NDAs, for, among other things, new indications, dosage forms, or strengths of an existing drug, if new clinical investigations that were conducted or sponsored by the applicant are essential to the approval of the application.

IPLEX is currently protected by 3-year exclusivity, which expires on December 12, 2008. This exclusivity runs concurrently with a 7-year period of orphan drug exclusivity, which prevents the FDA from approving another marketing application for the same drug for the same indication, except in the limited circumstances described below. In addition, the FDA s Orange Book publication lists two patents covering IPLEX to which a generic applicant must certify.

Orphan Drug Designation and Exclusivity

Some jurisdictions, including Europe and the United States, may designate drugs for relatively small patient populations as Orphan Drugs. The FDA grants Orphan Drug Designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or in cases where more than 200,000 individuals are affected in the United States, for which there is no reasonable expectation that the cost of developing and making such drugs available in the United States will be recovered from sales in the United States. In the United States, Orphan Drug Designation must be requested before submitting an application for marketing approval. 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 FDA approval for the indication for which it has such designation, the product is entitled to Orphan Drug Exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of 7 years, except in limited circumstances. After an orphan drug is approved, the FDA can subsequently approve a competitor s version of the same drug for the same indication if the subsequent applicant shows clinical superiority (superior efficacy, safety, or a major contribution to patient care) to the approved product with Orphan Drug Exclusivity. Also, competitors may receive approval of different drugs or biologics for the indications for which the Orphan Drug has exclusivity.

IPLEX was approved on December 12, 2005 as an Orphan Drug, and is currently protected by 7-year Orphan Drug Exclusivity for the treatment of Severe Primary IGFD. This exclusivity expires on December 12, 2012. This period of exclusivity runs concurrently with the 3-year period of exclusivity applicable to IPLEX. We have received Orphan Drug Designation for IPLEX for the treatment of extreme insulin resistance. We also intend to file for Orphan Drug Designation for other indications that meet the criteria for Orphan Drug Designation. If the FDA designates the drug and approves our marketing application, or approves marketing applications under current designations, we will be granted seven years of Orphan Drug Exclusivity for the drug for the designated indication. Obtaining FDA approval to market a product with Orphan Drug Exclusivity may not provide us with a material commercial advantage.

Under European Union medicines laws, the criteria for designation as an orphan medicine are similar to those in the United States. A drug is designated as an Orphan Drug if the sponsor can establish that the drug is intended for a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the European Union or that is unlikely to be profitable, and if there is no approved satisfactory treatment or if the drug would be a significant benefit to those persons with the condition. Orphan medicines are entitled to ten years of market exclusivity, except under certain limited circumstances comparable to U.S. law. During this period of market exclusivity, no similar product, whether or not supported by full safety and efficacy data, will be approved unless a second applicant can establish that its product is safer, more effective or otherwise clinically superior. This period may be reduced to six years if the conditions that originally justified Orphan Drug Designation change or the sponsor makes excessive profits. We have been granted Orphan Drug Designation by the EMEA for IPLEX in the treatment of growth disturbance due to growth hormone insensitivity syndrome (Laron Syndrome). We have also obtained Orphan Drug Designation in the European Union for IPLEX for the treatment of extreme insulin resistance.

Table of Contents

Other Regulatory Requirements

We are also subject to a number of post-approval regulatory requirements. If we seek to make certain changes to an approved product, such as promoting or labeling a product for a new indication, making certain manufacturing changes or product enhancements or adding labeling claims, we will need FDA review and approval before the change can be implemented. While physicians may use products for indications that have not been approved by the FDA, we may not label or promote the product for an indication that has not been approved. Securing FDA approval for new indications or product enhancements and, in some cases, for manufacturing and labeling claims, is generally a time-consuming and expensive process that may require us to conduct clinical studies under the FDA s IND regulations. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all. In addition, adverse experiences associated with use of the products must be reported to the FDA, and FDA rules govern how we can label, advertise or otherwise commercialize our products.

There are current post-marketing safety surveillance requirements that we need to meet to continue to market an approved product. The FDA also may, in its discretion, require post-marketing testing and surveillance to monitor the effects of approved products or place conditions on any approvals that could restrict the commercial applications of these products.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal health care program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid or other federally financed health care programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal health care programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other health care companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn are used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we and our manufacturers are subject to requirements that drugs be manufactured, packaged and labeled in conformity with current good manufacturing practice, or cGMP. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, record-keeping and other requirements. The FDA periodically inspects drug manufacturing facilities to evaluate compliance with cGMP requirements.

Also, as part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. This practice is regulated by the FDA and other governmental authorities, including, in particular, requirements concerning record-keeping and control procedures.

Table of Contents

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 studies 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

At December 31, 2005, we had 85 employees, including 17 in research and development, 23 in regulatory, clinical and quality assurance, 28 in manufacturing and 17 in finance and administration. In connection with the commercial launch of IPLEX and to create a sufficient sales and marketing capability for the commercialization of other drug and other indications, once approved, we expect to hire approximately 40 additional employees in our Sales and Marketing department by December 31, 2006. We also expect to hire approximately 40 additional employees for manufacturing operations in Boulder, Colorado.

Our continued success will depend in large measure on our ability to attract and retain highly skilled employees who are in great demand. None of our employees are represented by a labor union, and we believe that our relations with the employees are generally good.

Facilities

Our Headquarters is located in Glen Allen, Virginia where we occupy approximately 46,000 square feet of space for corporate and development activities under a lease expiring in October 2006.

Our manufacturing facility is located in Boulder, Colorado where we occupy approximately 25,000 square feet dedicated to cGMP production of commercial and clinical drug and quality control and 26,000 square feet of space in two adjacent facilities for additional laboratory and research and development operations, administrative functions, and cGMP warehouse and dispensing operations. Our lease for the Boulder facility dedicated to cGMP manufacturing expires in February 2008 but may be renewed annually for up to an additional 5 years.

Table of Contents

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Lazard Capital Markets LLC is the representative of the underwriters.

Underwriter	Number of Shares
Lazard Capital Markets LLC	
C.E. Unterberg, Towbin, LLC	
Total	20,000,000

The underwriters are committed to purchase all of the shares of common stock offered by this prospectus supplement, other than those covered by the over-allotment option described below, if any of these shares are purchased.

We have granted to the underwriters an option, exercisable not later than 30 days after the date of this prospectus supplement, to purchase up to 3,000,000 additional shares of common stock at the public offering price, less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement. The underwriters may exercise this option only to cover over-allotments made in connection with the sale of the common stock offered by this prospectus supplement. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the table above bears to the total number of shares of common stock listed in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise by the underwriters of their over-allotment option.

	Total	
	Without Exercise of Over-Allotment	With Full Exercise of Over-Allotment
Per share	$	$
Total	$	$

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a price that represents a concession not in excess of $ per share from the initial public offering price. Any such securities dealers may resell any shares purchased from the underwriters to certain other brokers or dealers at a discount of up to $ per share from the initial public offering price. After the initial offering of the shares of our common stock, the offering price and other selling terms may from time to time be varied by the representatives.

Expenses of the Offering

We estimate that the net total expenses of the offering, excluding the underwriting discounts and commissions, will be approximately $.

Table of Contents

No Sales of Similar Securities

We and each of our directors and executive officers have agreed that, without the prior written consent of Lazard Capital Markets LLC on behalf of the underwriters, we and they will not, during the period ending 90 days after the date of this prospectus supplement:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock;

whether any transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, our directors and executive officer have agreed that, without the prior consent of Lazard Capital Markets LLC on behalf of the underwriters, they will not, during the period ending 90 days after the date of this prospectus supplement, make any demand for, or exercise any right with respect to, the registration of any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock.

The restrictions described in the preceding paragraph do not apply to:

- the sale of shares to the underwriters pursuant to the underwriting agreement;

- the grant of options to purchase common stock and the issuance of shares of common stock to our officers, directors and employees pursuant to our equity plans;

- transfers of shares or any security convertible into our common stock as a bona fide gift, or to a family trust, or pursuant to the rules of descent and distribution; or

- transfers of shares or any security convertible into our common stock between or among affiliated stockholders or distributions by a stockholder of shares or any security convertible into our common stock to limited partners or stockholders of the stockholder;

provided that, in the case of each of the last two transactions, each recipient agrees to accept the restrictions described in the immediately preceding paragraph and no filing under the Exchange Act is required, during the 90-day restricted period, in connection with these transactions.

The 90-day restricted period described in the two preceding paragraphs is subject to extension such that, in the event that either (1) during the period that is 15 calendar days plus three business days prior to the end of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the lock-up restrictions described above will continue to apply until the expiration of 15 calendar days plus three business days after the issuance of the earnings release or the occurrence of the material news or material event.

The Nasdaq National Market Listing

Our common stock is quoted on The Nasdaq National Market under the symbol INSM.

Short Sales, Stabilizing Transactions and Penalty Bids

In order to facilitate this offering, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock during and after this offering. Specifically, the underwriters may engage in the following activities in accordance with the rules of

the Securities and Exchange Commission.

Table of Contents

Short sales. The underwriters may sell a greater number of shares than they are required to purchase in the offering, creating a short position. Covered short sales are short sales made in an amount not greater than the underwriters over-allotment option to purchase additional shares from us in this offering. The underwriters may close out any covered short position by either exercising their over-allotment option to purchase shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

Stabilizing transactions. As an additional means of facilitating the offering, the underwriters may make bids for or purchases of the shares for the purpose of pegging, fixing or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

Penalty bids. The underwriters may also impose a penalty bid. This occurs when underwriting syndicate reclaims selling concessions allowed to an underwriter or a dealer for distributing the common stock in the offering, if the syndicate repurchases previously distributed common stock to cover syndicate short positions or to stabilize the price of the common stock. Stabilization and syndicate covering transactions may cause the price of the shares to be higher than it would be in the absence of these transactions. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages presales of the shares.

The transactions above may occur on The Nasdaq National Market or otherwise. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. If these transactions are commenced, they may be discontinued without notice at any time.

Indemnification of the Underwriters

We will indemnify the underwriters against some civil liabilities, including liabilities under the Securities Act and liabilities arising from breaches of our representations and warranties contained in the underwriting agreement. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

Investment Banking Services Provided by the Underwriters

In the ordinary course of its business, certain of the underwriters and their respective affiliates have, from time to time, provided or may in the future provide investment banking or other financial advisory services to us, for which they have received or will receive customary fees and commissions.

Table of Contents

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Woods Rogers PLC. Goodwin | Procter LLP will pass upon certain other legal matters relating to the offering for Insmed. Dechert LLP will pass upon certain legal matters relating to the offering for the underwriters.

Table of Contents

PROSPECTUS

INSMED INCORPORATED

$75,000,000

Common Stock

Preferred Stock

Warrants

This prospectus relates to common stock, preferred stock and warrants that we may sell from time to time in one or more offerings up to an aggregate public offering amount of $75,000,000 (or its equivalent in foreign or composite currencies) on terms to be determined at the time of sale. We will provide specific terms for any sale of the securities in one or more supplements to this prospectus. You should read this prospectus and any applicable supplement, as well as the documents incorporated or deemed to be incorporated by reference in this prospectus, carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for the securities.

Our common stock is listed on The Nasdaq National Market under the trading symbol INSM. Each prospectus supplement to this prospectus will contain information, where applicable, as to any listing on The Nasdaq National Market or any securities market or exchange of the securities covered by the prospectus supplement.

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See Plan of Distribution in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds that we expect to receive from any such sale will also be included in a prospectus supplement.

An investment in our securities involves a high degree of risk. You should consider carefully the Risk Factors beginning on page 4 of this prospectus. We may also include additional risk factors in an applicable prospectus supplement under the heading Risk Factors. You should review that section of the prospectus supplement for a discussion of matters that investors in our securities should consider.

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

The date of this prospectus is February 14, 2006

Table of Contents

Table of Contents

You should rely on the information contained in this prospectus, any prospectus supplement or any document incorporated herein or therein to which we have referred you. We have not authorized anyone to provide you with information that is different. This prospectus and any prospectus supplement may be used only where it is legal to sell these securities. The information contained in this prospectus or any prospectus supplement is accurate only as of the date on the front of these documents, regardless of the time of delivery of this prospectus or of any sale of our securities.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus. This summary may not contain all of the information that is important to you. You should read the entire prospectus and the applicable prospectus supplement carefully, including Risk Factors beginning on page 4 of this prospectus, before deciding to invest in our securities.

About this Prospectus

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total public offering price of $75,000,000 (or its equivalent in foreign or composite currencies). This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the securities being offered and the terms of that offering. The prospectus supplement may also add to, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described under the heading Where You Can Find More Information carefully before making an investment decision.

Unless the context otherwise requires, in this prospectus, Insmed, we, us and our refer to Insmed Incorporated and its subsidiaries.

About Insmed

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-1 activity in the human body. We currently have one drug that has been approved for commercial sale by the United States Food and Drug Administration (FDA), IPLEX (mecasermin rinfabate (rDNA origin) injection), and two other lead drug candidates, rhIGFBP-3 and INSM-18. We are also developing these drugs to treat indications in the metabolic and oncology fields.

On December 12, 2005, the FDA approved IPLEX (mecasermin rinfabate (rDNA origin) injection) for the treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. We have been granted Orphan Drug Designation by the FDA and European Medicines Agency for the Evaluation of Medicinal Products (EMEA) for IPLEX in the treatment of severe growth disturbance due to growth hormone insensitivity syndrome (GHIS) (i.e., Laron s Syndrome). As an orphan drug, IPLEXs entitled to seven years of marketing exclusivity for the treatment of Primary IGFD in the United States and should approval be granted by the EMEA, IPLEX may be granted 10 years of marketing exclusivity in the European territory. Our worldwide Phase III clinical trial for this indication will continue for an additional two years and will assess immunogenicity.

We believe the commercial opportunities for IPLEX reach beyond the indication of Primary IGFD and that initial approval of IPLEX may offer us an opportunity to enter, in the future when we have conducted full clinical studies, other potentially large markets. These markets include other growth disturbances related to IGF-1 deficiency, severe insulin resistance, diabetes, myotonic dystrophy, HIV associated adipose redistribution syndrome, severe burns, hip fracture and retinopathy of prematurity. It is our intention to initiate clinical studies in a variety of these indications with IPLEX. 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

Table of Contents

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 has also initiated clinical study of a small molecule compound known as INSM-18, which has novel effects on the activity of the IGF-1 and other receptors that can lead to the inhibition of growth of various tumors. Insmed is currently conducting the study and 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 Information

Insmed was incorporated in the Commonwealth of Virginia on November 29, 1999. Our principal executive offices are located at 4851 Lake Brook Drive, Glen Allen, Virginia 23060 and our phone number is (804) 565-3000. Our internet address is *www.insmed.com*. We make available on our Internet website free of charge a link to our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports as soon as practicable after we electronically file such material with the SEC. Information contained on our website is not incorporated into this prospectus and is not a part of this prospectus.

The Securities We May Offer

We may offer shares of our common stock, preferred stock and warrants to purchase common stock or preferred stock with a total value of up to $75,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate offering price;
- rates and times of payment of dividends or other payments, if any;
- redemption, conversion, preemption, exchange, settlement or sinking fund terms, if any;
- conversion, exchange or settlement prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion, exchange or settlement prices or rates and in the securities or other property receivable upon conversion, exchange or settlement;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and

important federal income tax considerations.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

Table of Contents

We may sell the securities directly or through underwriters, dealers or agents. We, and our underwriters, dealers or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters, dealers or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote per share for the election of directors and on all other matters that require shareholder approval. Subject to any preferential rights of any then outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets remaining after payment of liabilities and the liquidation preferences of any then outstanding preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock, or any redemption rights.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors has the authority, without further action by shareholders, to designate up to 200,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of the common stock. To date, of the 200,000,000 authorized shares of preferred stock, our board of directors has designated 500,000 shares as Series A Junior Participating Preferred Stock.

We will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplements related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Warrants. We may issue warrants for the purchase of common stock and/or preferred stock in one or more series, from time to time. We may issue warrants independently or together with common stock and/or preferred stock, and the warrants may be attached to or separate from those securities.

The warrants will be evidenced by warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the prospectus supplements related to the series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of warrant agreements and warrant certificates relating to warrants for the purchase of common stock and preferred stock have been filed as exhibits to the registration statement of which this prospectus is a part, and complete warrant agreements and warrant certificates containing the terms of the warrants being offered will be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

Table of Contents

RISK FACTORS

You should consider carefully the following risk factors, together with all of the other information included in this prospectus or incorporated by reference into this prospectus. 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.

Until recently we have been focused solely 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 September 30, 2005, our accumulated deficit was $242 million. For the nine months ended September 30, 2005 our consolidated net loss was $28 million.

We have one drug that was recently approved for commercial sale, IPLEX (mecasermin rinfabate (rDNA origin) injection)) for the treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH, and we are in the earlier stages of researching and developing two other lead drug candidates, rhIGFBP-3 and INSM-18. IPLEX is also in development for other metabolic and endocrine indications. rhIGFBP-3 and INSM-18 are currently in pre-clinical and clinical development for a variety of cancers including breast, lung, colon and prostate.

All of our products are currently in, or have just completed, the research and development stage. 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, or have just completed, the research and development stage. Our long-term viability and growth depend on the successful development and 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).

Table of Contents

The development program with respect to any given product will take many years and thus delay our ability to generate profit. In addition, potential products that appear promising at early stages of development may fail for a number of reasons, including the possibility that the products may require significant additional testing or turn out to be:

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

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

- raise sufficient money to pay for the development;
- attract and retain appropriate personnel; and
- develop relationships with other companies to perform various development activities that we are unable to perform.

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

- the regulatory 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 lawsuit or other litigation drains our cash;
- we are unable to manufacture the quantity of product needed in accordance with current good manufacturing practices to meet market demand or at all,

our product is determined to be ineffective or unsafe following approval and is removed from the market or we are required to perform additional research and development to further prove the safety and effectiveness of the product before re-entry into the market,

competition from other products or technologies prevents or reduces market acceptance of our products;

we do not have and cannot obtain the intellectual property rights needed to manufacture or market our products without infringing on another company s patents, or

we are unable to obtain reimbursement for our product 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.

Table of Contents

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

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

We are currently conducting a Phase III clinical trial of IPLEX in patients with severe Primary IGFD and plan to include the data from the trial in a Marketing Authorization Application (MAA) to the European Medicines Agency (EMEA). We must receive approval of these applications before we can market IPLEX in certain countries outside of the United States. We are also planning and conctucting clinical trials with rhIGFBP-3 and INSM-18.

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 IPLEX 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-1, concerns were raised that long-term use of rhIGF-1 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-1, the United States Food and Drug Administration (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 or prevent our commercialization of IPLEX for these broader chronic indications. Adverse results in these trials could prevent our commercialization of IPLEX for broad chronic indications or could jeopardize existing development and approvals in other indications.

6

Table of Contents

We cannot be certain that we will obtain additional 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.

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 IPLEX in patients with severe Primary IGFD and plan to include the data in a MAA submission to the EMEA. We must receive approval of these applications before we can market IPLEX in certain countries outside of the United States. We also must submit results of this study, particularly regarding immunogenicity, to the FDA as agreed for the approval of IPLEX.

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 and for commercialization is essentially the same as the new drug product produced. We have had several discussions with the FDA and intend to have discussions with foreign regulatory agencies regarding our Phase III clinical study and this comparability analysis. We believe we understand what is required to satisfy the EMEA. We plan to submit this data to the appropriate regulatory authorities as part of the regulatory process. If we do not properly understand what is required to satisfy regulatory authorities or 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 IPLEX. If the EMEA does 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 the 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 the 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

Table of Contents

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 FDA and/or EMEA 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 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 the 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 product candidates. 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 a product we are developing in a particular indication, we may be precluded or delayed from commercializing the product 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, even if our product is approved and receives orphan drug status, like our drug IPLEX, the FDA can still approve different drugs for use in treating the same indication or disease covered by our product, which could create a more competitive market for us.

The grant of orphan drug market exclusivity or pediatric drug market exclusivity to a competitor for a drug that we are currently developing in the same indication will adversely affect our business, financial condition and results of operations.

Manufacturing capacity necessary to supply IPLEX 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 or successfully develop our own manufacturing capabilities, 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 our Insmed Therapeutic Proteins (ITP)

Table of Contents

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.

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 IPLEX 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 IPLEX at our ITP facility and at Avecia s site at Billingham, England. At present, IPLEX has never been manufactured by Avecia in quantities necessary for commercialization; we cannot guarantee that ITP or Avecia will be able to produce the quantities of IPLEX necessary for commercialization or that there will not be delays in such production. If we are unable to manufacture IPLEX 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 IPLEX must undergo inspections by the FDA and/or the EMEA for compliance with cGMP regulations, both before and after IPLEX approval. 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 additional approvals for IPLEX. In addition, ITP, our contract manufacturers, and any alternative contract manufacturer we may utilize, will be subject to ongoing periodic inspection by the FDA and the 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 our ITP manufacturing facility and then sent to an additional third party contract manufacture for sterile filtration and filling into vials. Should our ITP 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 IPLEX or validation of the manufacturing process for IPLEX. This could delay our clinical trials and the approval of our 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 IPLEX 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 IPLEX 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 IPLEX , or higher costs of production and result in our failure to effectively commercialize IPLEX.

Table of Contents

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 IPLEX. and we would lose potential revenues.

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

Now that the FDA has permitted us to commence commercial sales of IPLEX, we 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 there are fewer children with severe Primary IGFD deficiency than we estimate, we may not generate sufficient revenues to continue development of other products or to continue operations, or we may not be able to complete our clinical trials.

If there are fewer children with severe Primary IGFD deficiency than we estimate, we may not generate sufficient revenues to continue development of other indications or products and may cease operations. We estimate that the number of children in the United States with Primary IGFD is approximately 6,000. Our estimate of the size of the patient population is based on our interpretation of published studies. If our interpretation and extrapolation of data from these published studies do not accurately reflect the number of children with Primary IGFD, our assessment of the market may be incorrect, making it difficult or impossible for us to meet our revenue goals.

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 approved product and 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 after 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.

Table of Contents

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

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

Changes and reforms in the health care system or reimbursement policies may adversely affect the sale of our future products or our ability to obtain an adequate level of reimbursement or acceptable prices for our future products.

Our ability to earn sufficient returns on our products, if and when such products are approved and ready for marketing, will depend in part on the extent to which reimbursement for our products and related treatments will be available from government health administration authorities, private health coverage insurers, managed care organizations and other third-party payers. If we fail to obtain appropriate reimbursement, it could prevent us from successfully commercializing our future products.

There have been and continue to be efforts by governmental and third-party payers to contain or reduce the costs of health care through various means, including limiting coverage and the level of reimbursement. We expect that there will continue to be a number of legislative proposals to implement government controls and other reforms to limit coverage and reimbursement. The announcement of these proposals or reforms could impair our ability to raise capital. The adoption of these proposals or reforms could impair our operations and financial condition.

Additionally, third-party payers, including Medicare, are increasingly challenging the price of medical products and services and are limiting the reimbursement levels offered to consumers for these medical products and services. If purchasers or users of our future products are not able to obtain adequate reimbursement from third-party payers for the cost of using these products, they may forego or reduce their use. Significant uncertainty exists as to the reimbursement status of newly approved health care products, including gene therapy treatments, and whether adequate third-party coverage will be available.

We cannot provide any assurance that third-party payers will provide adequate reimbursement, if any, for IPLEX.

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;

Table of Contents

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 do not believe that existing cash reserves, including amounts raised in our 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. For example, in August 2005, our Chief Financial Officer resigned to work for a medical company. We cannot assure that we will attract and retain appropriate persons or maintain such relationships.

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

We need collaborative relationships to be successful. If we are unable to form these relationships it could 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 product;

disputes may arise in the future with respect to the ownership of rights to technology developed with, licensed to or licensed from corporate partners;

Table of Contents

- 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 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;

Table of Contents

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-1 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 IPLEX or rhIGFBP-3. We can give no assurances that such patents 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., Tercica, Novartis, Ciba-Geigy, Cephalon, Pharmacia(Pfizer), Fujisawa, Amgen, and Chiron Corporation hold United States and/or foreign patents possibly directed to the composition, production and/or use of rhIGF-1, rhIGFBP-3, IPLEX and/or recombinant proteins in general. After examining these patents, we do not believe they present an obstacle to our plans to commercialize IPLEX and rhIGFBP-3 or INSM-18. 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 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-growth hormone-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 IPLEX for certain indications, and may expose us to liability for induced infringement for off-label use of IPLEX.

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

Table of Contents

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.

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-1. 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. A trial date in this litigation has not been set.

In addition, on December 23, 2004, Genentech Inc. and Tercica Inc. sued Insmed for infringement of two U.S. Patents 5,187,151 and 6,331,414. These patents are directed to certain methods of using IGF-1/IGFBP-3 and methods of producing human IGF-1, respectively. On February 16, 2005, Tercica filed an amended complaint, adding an infringement allegation against Insmed with respect to U.S. Patent No. 5,528,287. 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. We moved to dismiss the amended complaint for lack of jurisdiction and on other grounds. At a hearing on the motion on April 15, 2005, the court granted our motion and dismissed the case with leave for plaintiffs to refile the complaint. A Second Amended Complaint was filed on April 22, 2005 by Genentech Inc. and Tercica Inc. against Insmed. We moved to dismiss the portion of the Second Amended Complaint that relates to U.S. Patent No. 5,528,287. On June 29, 2005, the Court denied our motion to dismiss. On July 14, 2005, Insmed filed its Answer and Counterclaims. In the Answer and Counterclaims, we denied infringement and seeks a declaratory judgment that the asserted patents are not infringed, are invalid, and/or are unenforceable. Plaintiffs Reply to the Counterclaims was filed on August 5, 2005. On October 17, 2005, Tercica and Genentech filed a Third Amended Complaint adding Insmed Therapeutic Proteins as a Defendant. The Answer and Counterclaims in response to the Third Amended Complaint were filed by us on October 27, 2005. Discovery is ongoing and a trial date is scheduled for November 2006.

On May 27, 2005, plaintiffs filed a motion for preliminary injunction seeking an order barring Insmed, until trial, from making, using or selling the drug called SomatoKine, (now known as IPLEX) with respect to its

Table of Contents

allegations of infringement of U.S. Patent Nos. 6,331,414 and 5,187,151, and requesting that Insmed be required to share any orphan drug exclusivity it obtains with Tercica. We filed our opposition to the motion for a Preliminary Injunction on June 10, 2005. On June 16, 2005, plaintiffs withdrew their motion for a preliminary injunction. The case is now in discovery.

Insmed cannot predict with certainty the outcome of proceedings involving Tercica, Inc. or Genetech, Inc. An adverse ruling on any of the claims alleged could seriously impact our ability to make, use or sell our products and may have a material adverse effect on our business, financial condition and results of operations.

We are currently a defendant in a pending civil action. An unfavorable settlement or judgment in this action could harm our business and financial condition.

On December 6, 2005, with an Amendment on December 15, 2005, Tercica Inc. filed a lawsuit in U.S. District Court for the Northern District of California against Insmed alleging deceptive promotional statements and unfair business practices related to Tercica, Inc. s product, IncrelexThe complaint alleges that Insmed has publicly disseminated unlawful information in violation of the California Business and Professions Code and the Federal Lanham Act. Tercica is requesting injunctive and monetary relief.

Although Insmed denies any liability and believes that Tercica, Inc. s true motive in filing the action is to inappropriately damage Insmed, no assurances can be given as to the outcome of this action. An unfavorable settlement or decision in this action could negatively affect our operations and financial condition. Any liability resulting from this action may exceed our financial resources. Discovery has not initiated in this action and no trial date has been set.

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 our leading product was only recently approved for commercial sale and our other products are under development, we cannot predict the relative competitive position of our products. However, we expect that the following factors, among others, will determine our ability to compete effectively:

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

16

Table of Contents

Currently, we are aware of at least one other company, Tercica, Inc., that has received approval from the FDA for a product for this indication or a similar indication. Tercica, Inc. s product was approved for the long term treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. We believe this indication would include patients with GHIS. We also believe Tercica may also be planning to develop rhIGF-1 for some of the same indications that we plan to pursue with IPLEX.

Growth hormone may also be a competitive product for the treatment of some indications that we may pursue with IPLEX such as HIV associated adipose redistribution syndrome. 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-1 deficiency. We are also aware that Serono is seeking regulatory approval for their growth hormone, Serostim, for the treatment of HIV associated adipose redistribution syndrome. We are also aware that Theratechnologies is conducting Phase III trials for a growth hormone releasing agonist 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 IPLEX.

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, inhalable insulin, GLP-1 analogues and oral hypoglycemic drugs.

Further, 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 three products, Symlin, Byetta, and a long-acting release (LAR) formulation of Byetta, for the treatment of type 2 diabetes. Symlin and Byetta were recently approved for use by the FDA. Tercica, Inc. has indicated that it plans to pursue the development of rhIGF-1 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 IGF-1 pathway as rhIGFBP-3. These companies include Imclone, Amgen, OSI Pharmaceuticals, Bristol-Meyer Squibb and Genentech.

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.

Table of Contents

Competitors could develop and gain FDA approval of products containing rhIGF-1, which could adversely affect our competitive position in all indications where we are currently developing IPLEX

rhIGF-1 manufactured by other parties may be approved for use in other indications in the United States in the future, including severe insulin resistance, myotonic muscular dystrophy and HIV associated adipose redistribution syndrome. In the event there are other rhIGF-1 products approved by the FDA to treat indications other than those covered by IPLEX , physicians may elect to prescribe a competitor s product containing rhIGF-1 to treat the indications for which IPLEX has received and may receive approval. This is commonly referred to as off-label use. While under FDA regulations a competitor is not allowed to promote off-label use of its product, the FDA does not regulate the practice of medicine and as a result cannot direct physicians as to what product containing rhIGF-1 to prescribe to their patients. As a result, we would have limited ability to prevent off-label use of a competitor s product containing rhIGF-1 to treat any diseases for which we have received FDA approval even if it violates our patents and/or we have orphan drug exclusivity for the use of rhIGF-1 to treat such diseases.

It is illegal for Insmed to promote IPLEX for uses other than those approved by the regulatory authorities. Such off-label promotion, as it is known, may result in regulatory actions against Insmed even if such activities by Insmed are inadvertent.

Physicians may prescribe drugs for uses that are not described in the product s labeling and that differ from those approved by the FDA. Such off-label uses are common across medical specialties. Although the FDA does not regulate the practice of medicine, the FDA does restrict manufacturers communications with respect to off-label use. Companies cannot promote FDA-approved drugs for off-label uses; a company may engage in truthful, non-misleading, and non-promotional speech concerning its products. For example, while we may inform physicians that we are conducting a clinical trial to evaluate the safety and effectiveness of IPLEX in unapproved uses and encourage those physicians to refer eligible patients to enroll in the clinical trial, we cannot promote that the product is effective for unapproved uses. We may also educate physicians about a particular disease state and how that disease is properly diagnosed so that patients who qualify for the clinical trial might be identified, and survey physicians who are lawfully prescribing our products or competitors products for off-label uses to monitor patients experiences. We may also, pursuant to FDA policies, respond to unsolicited requests from health care professionals and engage in appropriate scientific exchange of information about unapproved uses. As we have no sales and marketing experience, we have not engaged in these lawful activities in the past. Our sales and marketing employees may not understand the regulations against off-label promotion. We do not yet have policies and procedures in place to regulate the lawful promotion of our marketed products within their labeled indications. However, employees will be trained to follow specific policies and procedures designed to instruct the lawful promotion of our products and must certify that they will abide by them. We cannot guarantee that our employees will follow these policies and procedures. The FDA actively enforces regulations prohibiting promotion of off-label uses and the promotion of products for unapproved uses. The FDA s regulations and policies are subject to varying interpretations, which are evolving. We cannot guarantee that we will change our policies as the FDA s regulations and policies change. Failure to comply with these regulations and policies in the past or with respect to future activities can result in regulatory enforcement action by the FDA and other governmental bodies, which would have an adverse effect on our revenues, business and financial prospects.

Competitors could develop and gain FDA approval of products containing rhIGF-1, which could adversely affect our competitive position.

We are aware of one other company currently marketing rhIGF-1 in the United States for a human therapeutic indication rhIGF-1 manufactured by other parties may be approved for use in the United States in the future. In the event there are other rhIGF-1 products approved by the FDA to treat indications other than those covered by Increlex, physicians may elect to prescribe a competitor s product containing rhIGF-1 to treat the indications for which Increlex has received and may receive approval. This is commonly referred to as off-label use. While under FDA regulations a competitor is not allowed to promote off-label use of its product, the FDA does not regulate the practice of medicine and as a result cannot direct physicians as to what product containing

Table of Contents

rhIGF-1 to prescribe to their patients. As a result, we would have limited ability to prevent off-label use of a competitor s product containing rhIGF-1 to treat any diseases for which we have received FDA approval even if it violates our method of use patents and/or we have orphan drug exclusivity for the use of rhIGF-1 to treat such diseases.

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.

Conversion of our outstanding notes and exercise of warrants and options issued by Insmed will significantly dilute the ownership interest of existing shareholders.

As of January 31, 2006, the convertible notes issued by us on March 15, 2005 and the warrants issued by us in March 2005, November 2004 and July 2003 were convertible into and exercisable for up to approximately 11.2 million shares of our common stock, representing approximately 15% of the our then outstanding common stock.

As of January 31, 2006, our outstanding options to our employees, officers, directors and consultants were exercisable for up to 6.1 million shares of our common stock, representing approximately an additional 8% of our then outstanding common stock.

The conversion or exercise of some or all of our convertible notes, warrants and options will significantly dilute the ownership interests of existing shareholders. Any sales in the public market of the common stock issuable upon such conversion or exercise could adversely affect prevailing market prices of our common stock.

Table of Contents

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 regulation, reimbursement changes and governmental investigation or audits related to us or to our products,
- developments related to our patents or other proprietary rights or those of our competitors;
- changes in the position of securities analysts with respect to our stock; and/or
- operating results below the expectations of public market analysts and investors.

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

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, 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 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 holder of the common stock. The issuance of preferred stock could

Table of Contents

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 asking 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 106 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 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.

Our common stock may be thinly traded from time to time, which means large transactions in our common stock may be difficult to conduct in a short time frame.

On occasion we have a low volume of daily trades in our common stock on The Nasdaq National Market. Any large transactions in our common stock may be difficult to conduct and may cause significant fluctuations in the price of our common stock.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates.

Table of Contents

FORWARD-LOOKING INFORMATION

The matters discussed throughout this prospectus that are not historical facts are forward-looking and, accordingly, involve estimates, projections, goals, forecasts, assumptions and uncertainties that could cause actual results or outcomes to differ materially from those expressed in the forward-looking statements. This prospectus and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934 (the Exchange Act). Our actual results may differ materially from those projected in the forward-looking statements as a result of the risk factors set forth above. In particular, please review the sections captioned Management s Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the fiscal year ended December 31, 2004, as amended, and our Quarterly Reports on Form 10-Q for the periods ended March 31, 2005, June 30, 2005 and September 30, 2005, which report is incorporated herein by reference, and such section of any subsequently filed Exchange Act reports.

These forward-looking statements may include, but are not limited to:

- the failure to meet expectations with respect to our future performance;
- our dependence on collaborative relationships;
- pricing pressures and other competitive factors;
- our reliance on financial markets for future capital requirements;
- demand for and market acceptance of our products and services;
- the availability and extent of utilization of manufacturing capacity and raw materials;
- the uncertainties of litigation;
- successful development of products and services and the timing of product and service introductions;
- our ability to license certain technologies or maintain our license agreements;
- failure to comply with U.S. Food and Drug Administration requirements;
- our ability to develop and implement new technologies;
- our ability to protect our intellectual property;

changes in healthcare policy;

our ability to attract and retain qualified personnel;

the impact of new accounting policies; and

other risks and uncertainties, including those set forth or incorporated in this prospectus or any prospectus supplement, and those detailed from time to time in our filings with the SEC.

In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, expects, plans, anticipa believes, estimates, forecasts, projects, predicts, potential, and similar expressions intended to identify forward-looking statements. Forward-looking statements include all statements regarding commencement of clinical trials, expected financial position, results of operations, cash flows, dividends, financing plans, business strategies, operating efficiencies or synergies, budgets, capital and other expenditures, competitive positions, growth opportunities for our proposed products, plans and objectives of management, proposed relationships with third-party research organizations, manufacturers and suppliers and markets for our stock.

We caution you not to place undue reliance on these forward-looking statements, which speak only as of the date they were made. We do not undertake any obligation to publicly release any revisions to these

Table of Contents

forward-looking statements to reflect events or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in this prospectus in greater detail under the heading Risk Factors. In connection with forward-looking statements which appear in these disclosures, prospective purchasers of the shares offered hereby should carefully consider the factors set forth in this prospectus under Risk Factors. Also these forward-looking statements represent our estimates and assumptions only as of the date of this prospectus.

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we expect to use the net proceeds from the sale of these securities for research and development, product marketing, other general corporate purposes, which may also include acquisitions, investments, capital expenditures, repurchases of our capital stock, and for any other purposes that we may specify in any prospectus supplement. We may also invest the net proceeds temporarily in short-term securities until we use them for their stated purpose.

Table of Contents

DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK

This summary of the our capital stock is qualified in all respects by reference to our articles of incorporation and bylaws, that are incorporated by reference into the registration statement which includes this prospectus and, with respect to preferred stock, the certificate of designation which will be filed with the SEC for each series of preferred stock we may designate, if any.

We will describe in a prospectus supplement the specific terms of any common stock or preferred stock that we may offer pursuant to this prospectus. If indicated in a prospectus supplement, the terms of such common stock or preferred stock may differ from the terms described below.

Authorized Capital Stock

Presently our authorized capital stock consists of 500,000,000 shares of common stock and 200,000,000 shares of preferred stock. The authorized shares of common stock and preferred stock are available for issuance without further action by our shareholders, unless such action is required by applicable law or the rules of any stock exchange or automated quotation system on which our securities may be listed or traded. If the approval of our shareholders is not so required, our board of directors may determine not to seek shareholder approval.

Common Stock

As of January 31, 2006, we had 76,756,342 shares of common stock outstanding. Holders of our common stock are entitled to one vote in the election of directors and on all other matters submitted to a vote of shareholders. They are only entitled to receive dividends when, as and if declared by our board of directors out of funds legally available for distribution, subject to the prior rights of any holders of preferred stock then outstanding. Holders of our common stock have no conversion or redemption rights or sinking fund provisions and no preemptive or other rights to subscribe for other Insmed securities. In the event of our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive pro rata the assets of Insmed which are legally available for distribution, after payments of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding. Our common stockholders do not have cumulative voting rights in the election of directors. All of the outstanding shares of our common stock are fully paid and nonassessable.

Our common stock is listed on The Nasdaq National Market under the trading symbol INSM. Wachovia Bank, N.A. is the transfer agent and registrar for our common stock. Its address is 1525 West W.T. Harris Blvd., 3C3, Charlotte, NC 28262-8522.

Preferred Stock

As of January 31, 2006, we had no shares of preferred stock outstanding. The 200,000,000 shares of preferred stock authorized by our articles of incorporation may be issued in one or more series and with rights and preferences that may be fixed or designated by our board of directors without any further action by our shareholders. To date, of the 200,000,000 authorized shares of preferred stock, our board of directors has designated 500,000 shares as Series A Junior Participating Preferred Stock. The designation, powers, preferences, rights and qualifications, limitations and restrictions of the preferred stock of each additional series will be fixed by the certificate of designation relating to such series, which will specify the terms of the preferred stock, including:

- the designation of the series, which may be by distinguishing number, letter or title;
- the number of shares of the series, which number the board of directors may thereafter (except where otherwise provided in the preferred stock designation) increase or decrease (but not below the number of shares thereof then outstanding);
- whether dividends, if any, shall be cumulative or noncumulative and the dividend rate of the series;

Table of Contents

the dates on which dividends, if any, shall be payable;

the redemption rights and price or prices, if any, for shares of the series;

the terms and amount of any sinking fund provided for the purchase or redemption of shares of the series;

the amounts payable on shares of the series in the event of any voluntary or involuntary liquidation, dissolution or winding up of the affairs of Insmed;

the preemptive rights, if any, for shares of the series;

whether the shares of the series shall be convertible into shares of any other class or series, or any other security, of Insmed or any other corporation, and, if so, the specification of such other class or series or such other security, the conversion price or prices or rate or rates, any adjustments thereof, the date or dates as of which such shares shall be convertible and all other terms and conditions upon which such conversion may be made;

restrictions on the issuance of shares of the same series or of any other class or series; and

the voting rights, if any, of the holders of shares of the series, provided that no share of preferred stock of any series will be entitled to more than one vote per share of preferred stock.

If we issue a series of preferred stock in the future that has voting rights or preferences over our common stock with respect to the payment of dividends and upon our liquidation, dissolution or winding up, the rights of the holders of our common stock offered hereby may be adversely affected.

Certain Anti-Takeover Provisions in our Certificate of Incorporation and Bylaws

The following is a summary of certain provisions of Virginia law and our articles of incorporation and bylaws. This summary does not purport to be complete and is qualified in its entirety by reference to the corporate law of Virginia and our articles of incorporation and bylaws.

Articles of Incorporation and Bylaws

Our articles of incorporation and bylaws contain various provisions intended to promote the stability of our shareholder base and render more difficult certain unsolicited or hostile attempts to take us over that could disrupt Insmed, divert the attention of our directors, officers and employees and adversely affect the independence and integrity of our business.

Pursuant to our articles of incorporation, our directors are divided into three classes, with each class serving a three-year term and consisting as nearly as possible of one-third of the directors.

Our bylaws provide that a special meeting of shareholders may be called only by the chairman of the board, a majority of the entire board of directors or the president. Shareholders are not permitted to call, or to require that the board of directors call, a special meeting of shareholders. Our bylaws establish an advance notice procedure for shareholders to nominate candidates for election as directors or to bring other business before meetings of our shareholders.

Subject to Virginia law, our articles of incorporation generally may be amended by the affirmative vote of the holders of a majority of the outstanding votes entitled to be cast by each voting group entitled to vote. However, certain provisions of the articles of incorporation may only be amended or repealed by the affirmative vote of the holders of 75 percent of the outstanding votes entitled to be cast voting together as a single class. Our bylaws may be amended by the affirmative vote of a majority of the entire board of directors, unless otherwise required by the articles

of incorporation or Virginia law. If shareholder voting is required for an amendment to the bylaws, 75 percent of the then outstanding stock voting together as a single voting group must vote in the affirmative to approve the amendment.

Table of Contents

We are also subject to Virginia law regulating business combinations, defined to include a broad range of transactions, between Virginia corporations and interested shareholders, defined as persons who have acquired at least 10% of a corporation s stock without the prior approval of our board of directors. Under one statutory provision, subject to limited exceptions, a corporation may not engage in any business combination with any interested shareholder for a period of three years after the date such person became an interested shareholder unless a majority of our disinterested directors and holders of at least two-thirds of the outstanding voting shares other than shares beneficially owned by the interested person approve the transaction. Under a second statutory provision, Virginia law requires an interested shareholder to obtain the approval of disinterested shareholders before the interested person may exercise its voting rights with respect to the acquired shares. Under the Virginia statute, certain notice and informational filings and special shareholder voting and meeting procedures must be followed prior to consummation of the purchase of stock that will provide the interested shareholder with the power to vote in excess of 20%, 33% or 50% of our outstanding voting stock. Assuming compliance with notice and information filing requirements, the purchased stock will not provide the interested purchaser with any voting rights with respect to the stock until a majority of our outstanding disinterested shares vote to restore the voting rights to the purchased stock. The Virginia statutes contain provisions enabling a corporation to avoid their restrictions. We have not sought to elect out of the statutes. Therefore, the restrictions imposed by these statutes will apply to us and any applicable shareholders.

Rights Plan

Our board of directors has adopted a rights plan. As a result, we issued one purchase right for each outstanding share of common stock. One purchase right will also be issued for each additional share of common stock that we issue. The rights become exercisable if, without the prior approval of our board of directors, a person or group acquires 15% or more of our outstanding common stock or commences or announces a tender or exchange offer which would result in such ownership. Each right that becomes exercisable entitles the registered holder to purchase one one-thousandth of a share of our junior participating preferred stock at a purchase price of $35 per one-thousandth of a share, subject to adjustment.

If, after the rights become exercisable, we were to be acquired through a merger or other business combination transaction or 50% or more of our assets or earning power were sold, each right would permit the holder to purchase, for the purchase price, common stock of the surviving company having a market value of twice the purchase price.

The rights expire on May 16, 2011, unless earlier redeemed or exchanged by us. The purchase price payable and the shares of preferred stock issuable upon exercise of the rights are subject to adjustment as described in the rights plan. In addition, our board of directors retains the authority to redeem, at $0.01 per right, the rights at any time prior to the acquisition by a person or group of 15% or more of our outstanding common stock.

Table of Contents

DESCRIPTION OF WARRANTS

We may issue securities warrants for the purchase of preferred stock and/or common stock. Securities warrants may be issued independently or together with preferred stock and/or common stock and may be attached to or separate from any offered securities. Each series of securities warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The securities warrant agent will act solely as our agent in connection with the securities warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of securities warrants or beneficial owners of securities warrants. This summary of some provisions of the securities warrants is not complete. You should refer to the securities warrant agreement, including the forms of securities warrant certificate representing the securities warrants, relating to the specific securities warrants being offered for the complete terms of the securities warrant agreement and the securities warrants. That securities warrant agreement, together with the terms of securities warrant certificate and securities warrants, will be filed with the SEC in connection with the offering of the specific securities warrants.

The particular terms of any issue of securities warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies (including composite currencies) in which the price of such warrants may be payable;
- the amount and terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;
- the price at which the securities purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants will commence and the date on which such right shall expire;
- any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;
- if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;

information with respect to book-entry procedures, if any; and

any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants. The prospectus supplement relating to any warrants to purchase equity securities may also include, if applicable, a discussion of certain U.S. federal income tax and ERISA considerations.

Securities warrants for the purchase of preferred stock and common stock will be offered and exercisable for U.S. dollars only. Securities warrants will be issued in registered form only.

Each securities warrant will entitle its holder to purchase the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

Table of Contents

After the close of business on the expiration date, unexercised securities warrants will become void. We will specify the place or places where, and the manner in which, securities warrants may be exercised in the applicable prospectus supplement.

Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

Prior to the exercise of any securities warrants to purchase preferred stock or common stock, holders of the securities warrants will not have any of the rights of holders of the preferred stock or common stock purchasable upon exercise, including the purchase of preferred stock or common stock, the right to vote or to receive any payments of dividends on the preferred stock or common stock purchasable upon exercise.

Table of Contents

PLAN OF DISTRIBUTION

We may offer and sell the securities covered by this prospectus in one or more of the following ways, or any other way set forth in an applicable prospectus supplement, from time to time:

- to or through underwriters or dealers;
- directly to one or more purchasers;
- through agents; or
- through a combination of any such methods above described.

The prospectus supplement will set forth the terms of the offering of the securities covered by this prospectus, including:

- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any underwriting discounts or commissions or agency fees and other items constituting underwriters or agents compensation;
- the initial public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallowed or paid to dealers; and
- any securities exchanges or markets on which the securities may be listed.

Any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

If underwriters are used in an offering, we will execute an underwriting agreement with such underwriters and will specify the name of each underwriter and the terms of the transaction (including any underwriting discounts and other terms constituting compensation of the underwriters and any dealers) in a prospectus supplement. The securities may be offered to the public either through underwriting syndicates represented by managing underwriters or directly by one or more investment banking firms or others, as designated. If an underwriting syndicate is used, the managing underwriters will be specified on the cover of the prospectus supplement. If underwriters are used in the sale, the offered securities will be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time. Unless otherwise set forth in the prospectus supplement, the obligations of the underwriters to purchase the offered securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the offered securities if any are purchased.

We may authorize underwriters or other persons acting as our agents to solicit offers by institutions to purchase the securities subject to the underwriting agreement from us, at the public offering price stated in the applicable prospectus supplement, under delayed delivery contracts providing for payment and delivery on a specified date in the future. If we sell securities under these delayed delivery contracts, the applicable prospectus supplement would state that this is the case and would describe the conditions to which these delayed delivery contracts will be subject and the commissions payable for that solicitation.

We may grant to the underwriters options to purchase additional securities to cover over-allotments, if any, at the public offering price, with additional underwriting commissions or discounts, as may be set forth in a related prospectus supplement. The terms of any over-allotment option will be set forth in the prospectus supplement for those securities.

Table of Contents

If any underwriters are involved in the offer and sale, they may engage in transactions that maintain or otherwise affect the price of the securities. These transactions may include over-allotment transactions, purchases to cover short positions created by the underwriter in connection with the offering and the imposition of penalty bids in accordance with Regulation M under the Exchange Act. If an underwriter creates a short position in the securities in connection with the offering, i.e., if it sells more securities than set forth on the cover page of the applicable prospectus supplement, the underwriter may reduce that short position by purchasing the securities in the open market. In general, purchases of a security to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. As noted above, underwriters may also choose to impose penalty bids on other underwriters and/or selling group members. This means that if underwriters purchase securities on the open market to reduce their short position or to stabilize the price of the securities, they may reclaim the amount of the selling concession from those underwriters and/or selling group members who sold such securities as part of the offering.

Neither we nor any underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of such securities. In addition, neither we nor any underwriter make any representation that such underwriter will engage in such transactions or that such transactions, once commenced, will be discontinued without notice.

If dealers are used in an offering, we will sell the securities to the dealers as principals. The dealers then may resell the securities to the public at varying prices which they determine at the time of resale. We may solicit offers to purchase the securities directly and we may sell the securities directly to institutional or other investors, who may be deemed to be an underwriter within the meaning of the Securities Act with respect to any resales of those securities. The terms of these sales, including the terms of any bidding or auction process, if utilized, will be described in the applicable prospectus supplement. The names of the dealers and the terms of the transaction will be specified in a prospectus supplement.

The securities may be sold directly by us through agents we designate from time to time at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale. If agents are used in an offering, the names of the agents and the terms of the agency will be specified in a prospectus supplement. Unless otherwise indicated in a prospectus supplement, the agents will act on a best-efforts basis for the period of their appointment.

Dealers and agents named in a prospectus supplement may be deemed to be underwriters (within the meaning of the Securities Act) of the securities described therein. In addition, we may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any resales thereof.

Underwriters, dealers and agents may be entitled to indemnification by us against specific civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the underwriters or agents may be required to make in respect thereof, under underwriting or other agreements. The terms of any indemnification provisions will be set forth in a prospectus supplement. Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of business.

If so indicated in a prospectus supplement, we may authorize underwriters or other persons acting as our agents to solicit offers by institutional investors to purchase securities pursuant to contracts providing for payment and delivery on a future date. We may enter contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutional investors. The obligations of any institutional investor will be subject to the condition that its purchase of the offered securities will not be illegal at the time of delivery. The underwriters and other agents will not be responsible for the validity or performance of such contracts.

Table of Contents

Each series of securities will be a new issue of securities and will have no established trading market (other than our common stock). Any common stock sold pursuant to a prospectus supplement will be eligible for quotation and trading on The Nasdaq National Market, subject to official notice of issuance. Any underwriters to whom securities are sold by us for public offering and sale may make a market in the securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. The securities, other than the common stock, may or may not be listed on a national securities exchange or eligible for quotation and trading on The Nasdaq National Market.

In order to comply with the securities laws of some states, if applicable, the securities offered hereby will be sold in those jurisdictions only through registered or licensed brokers or dealers. In addition, in some states securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and complied with.

Table of Contents

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Woods Rogers PLC.

EXPERTS

The consolidated financial statements of Insmed appearing in Insmed s Annual Report (Form 10-K) for the year ended December 31, 2004, and Insmed management s assessment of the effectiveness of internal control over financial reporting as of December 31, 2004, included therein, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements and management s assessment are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements, and other information with the SEC. You may read and copy any documents we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-00330 for further information on the Public Reference Room. Our SEC filings are also available to the public on our web site at *http://www.insmed.com* or at the SEC s web site at *http://www.sec.gov*.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below, and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (other than Current Reports on Form 8-K containing only Regulation FD or Regulation G disclosure furnished under Item 9 or 12 of Form 8-K, unless otherwise indicated therein), until all the shares registered by this prospectus are sold. The documents we incorporate by reference are:

1. Our Annual Report on Form 10-K for the fiscal year ended December 31, 2004 (as amended on June 10, 2005);

2. Our Quarterly Reports on Form 10-Q for the three months ended March 31, 2005 (as amended June 10, 2005), June 30, 2005 and September 30, 2005;

3. Our Current Reports on Form 8-K, filed with the SEC on January 24, and January 13, 2006, and December 19, December 14, December 9, October 5, September 29, September 28, September 15, August 16, August 9, June 10, May 26, May 17, May 11, April 19, April 14, March 16, March 11, February 22 and January 3, 2005 (other than Current Reports on Form 8-K containing only Regulation FD or Regulation G disclosure furnished under Item 9 or 12 of Form 8-K, unless otherwise indicated therein).

4. The description of our common stock contained in our Registration Statement on Form 8-A, as filed with the SEC on June 1, 2000, including any amendment or report filed for the purpose of updating that description; and

Table of Contents

5. The description of our Preferred Stock Purchase Rights contained in our Registration Statement on Form 8-A, as filed with the SEC on May 17, 2001, as amended by our Registration Statement on Form 8-A/A, as filed with the SEC on March 17, 2005, and including any amendment or report filed for the purpose of updating that description.

We will provide to each person, including any beneficial owners, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents that have been incorporated by reference in this prospectus but not delivered with the prospectus. Request for such documents can be made by contacting us at that following address and telephone number:

Insmed Incorporated

Attention: Mr. Michael Duncan

4851 Lake Brook Drive

Glen Allen, Virginia 23060

Telephone: (804) 565-3000

Table of Contents

20,000,000 Shares

Common Stock

Prospectus Supplement

LAZARD CAPITAL MARKETS

C.E. UNTERBERG, TOWBIN

March , 2006