TERCICA INC
Form S-3
November 09, 2005
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As filed with the Securities and Exchange Commission on November 9, 2005

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

TERCICA, INC.

(Exact name of registrant as specified in its charter)

Delaware	**26-0042539**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**

2000 Sierra Point Parkway, Suite 400

Brisbane, CA 94005

(650) 624-4900

(Address, including zip code, and telephone number,

including area code, of Registrant s principal executive offices)

JOHN A. SCARLETT, M.D.

President and Chief Executive Officer

Tercica, Inc.

2000 Sierra Point Parkway, Suite 400

Brisbane, CA 94005

(650) 624-4900

(Name, address, including zip code, and telephone number,

including area code, of agent for service)

Copies to:

SUZANNE SAWOCHKA HOOPER, ESQ.

Cooley Godward LLP

Five Palo Alto Square

3000 El Camino Real

Palo Alto, CA 94306-2155

(650) 843-5000

Approximate date of commencement of proposed sale to the public:

From time to time after the effective date of this registration statement

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ¨

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities To Be Registered	Amount to be Registered(1)(2)	Proposed Maximum Offering Price Per Share(3)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee
Common Stock, $0.001 par value per share	6,296,912	$ 10.41	$ 65,550,853.92	$ 7,715.34

(1) Includes 260,000 shares of common stock that may be issued upon the exercise of a warrant.
(2) Pursuant to Rule 416 under the Securities Act, the shares being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.
(3) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457 under the Securities Act. The price per share and aggregate offering price are based on the average of the high and low prices of the registrant s common stock on November 7, 2005, as reported on the Nasdaq National Market.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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Subject to Completion, Dated November 9, 2005

The information in this prospectus is not complete and may be changed. The selling stockholder may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

PROSPECTUS

6,296,912 Shares

Common Stock

This prospectus relates to the resale of up to 6,296,912 shares of our common stock that we may issue to the selling stockholder listed in the section beginning on page 19 of this prospectus. The shares of common stock offered under this prospectus by the selling stockholder are issuable to Kingsbridge Capital Limited, or Kingsbridge, pursuant to a common stock purchase agreement between us and Kingsbridge, dated October 14, 2005, and a warrant we issued to Kingsbridge on that date. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholder.

The selling stockholder may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholder may sell its shares of common stock in the section entitled Plan of Distribution on page 20. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is traded on the Nasdaq National Market under the symbol TRCA. On November 8, 2005, the last reported sale price of our common stock was $10.19 per share.

Investing in our common stock involves risk. See Risk Factors beginning on page 4 of this prospectus.

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

The date of this prospectus is _____, 200__

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ABOUT THIS PROSPECTUS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the selling stockholder has not, authorized anyone to provide you with information different from that contained in this prospectus. The selling stockholder is offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where it is lawful to do so. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere or incorporated by reference into this prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus carefully, including the section entitled Risk Factors and the documents that we incorporate by reference into this prospectus, before making an investment decision.

TERCICA, INC.

We are a biopharmaceutical company focused on the development and commercialization of new therapeutics for the treatment of short stature and other related metabolic disorders. Our current product is Increlex , recombinant human insulin-like growth factor-1, or rhIGF-1. We licensed the rights of Genentech, Inc. to develop, manufacture and commercialize rhIGF-1 products for a broad range of indications, including short stature, worldwide. Our initial focus is on developing Increlex as a replacement therapy for primary IGF-1 deficiency, or Primary IGFD. We define the indication Primary IGFD to mean a child who has a height standard deviation score, or Height SDS, and an IGF-1 standard deviation score, or IGF-1 SDS, of less than minus two, and the indication severe Primary IGFD to mean a child who has a Height SDS and IGF-1 SDS of minus three or less, in each case in the presence of normal or elevated levels of growth hormone. We submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, in February 2005 seeking approval of long-term rhIGF-1 replacement therapy for severe Primary IGFD, based on Phase III clinical trial data. The FDA approved our NDA in August 2005 and granted Increlex seven years of orphan drug marketing exclusivity for the long-term treatment of growth failure in children with severe Primary IGFD. We are conducting two late-stage clinical trials for the use of rhIGF-1 in Primary IGFD.

We are in the development stage, have a limited operating history and may not be able to generate revenue or attain profitability. Since our inception, we have not generated any revenue from operations and have a history of significant losses. Given that we expect to incur substantial net losses to commercialize Increlex, it is unclear when, if ever, we will become profitable.

Tercica, Inc. was formed in December 2001 as a Delaware corporation. Our principal executive offices are located at 2000 Sierra Point Parkway, Suite 400, Brisbane, CA 94005. Our telephone number is (650) 624-4900, and our website is located at www.tercica.com. The information on our website is not part of this prospectus.

References in this prospectus to we, us and our refer to Tercica, Inc. and its subsidiary. We have applied for registration of the trademarks Increlex, Tercica and the Tercica logo in the United States.

EQUITY FINANCING FACILITY WITH KINGSBRIDGE

On October 14, 2005, we entered into a committed equity financing facility, or CEFF, with Kingsbridge, pursuant to which Kingsbridge committed to purchase, subject to certain conditions, up to $75.0 million of our common stock. In connection with the CEFF, we entered into a common stock purchase agreement and registration rights agreement with Kingsbridge, both dated October 14, 2005, and on that date we also issued a warrant to Kingsbridge to purchase 260,000 shares of our common stock at an exercise price of $13.12 per share. This warrant is exercisable beginning on April 14, 2006 and for a period of five years thereafter.

The common stock purchase agreement entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years, shares of our common stock for cash consideration up to an aggregate of $75.0 million, subject to certain conditions and restrictions. The shares of common stock that may be issued to Kingsbridge under the common stock purchase agreement and the warrant will be issued pursuant to an exemption from registration under the Securities Act of 1933, as amended, or the Securities Act. Pursuant to the registration rights agreement, we have filed a registration statement of which this prospectus is a part, covering the possible resale by Kingsbridge of any shares that we may issue to Kingsbridge under the common stock purchase agreement or upon exercise of the warrant. Through this prospectus, the selling stockholder may offer to the public for resale shares of our common stock that we may issue to Kingsbridge pursuant to the common stock purchase agreement, or that Kingsbridge may acquire upon exercise of the warrant.

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For a period of 36 months from the first trading day following the effectiveness of the registration statement of which this prospectus is a part, we may, from time to time, at our discretion, and subject to certain conditions that we must satisfy, draw down funds under the CEFF by selling shares of our common stock to Kingsbridge. The purchase price of these shares will be at a discount of up to ten percent from the volume weighted average price of our common stock for each of the eight trading days following our election to sell shares, or draw down under the CEFF. The discount on each of these eight trading days will be determined as follows:

VWAP*	PERCENT OF VWAP	(APPLICABLE DISCOUNT)
Greater than or equal to $14.00 per share	94%	(6)%
Greater than or equal to $7.50 per share but less than $14.00 per share	92%	(8)%
Greater than or equal to $3.00 per share but less than $7.50 per share	90%	(10)%

* As set forth in the common stock purchase agreement, VWAP means the volume weighted average price (the aggregate sales price of all trades of our common stock during each trading day divided by the total number of shares of common stock traded during that trading day) of our common stock during any trading day as reported by Bloomberg, L.P. using the AQR function. The VWAP and corresponding discount will be determined for each of the eight trading days during a draw down pricing period.

During the eight trading day pricing period for a draw down, if the VWAP for any one trading day is less than the greater of (i) $3.00 or (ii) 90 percent of the closing price of our common stock on the trading day immediately preceding the beginning of the draw down period, the VWAP for that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one-eighth of the draw down amount initially specified. In addition, if trading in our common stock is suspended for any reason for more than three consecutive or non-consecutive hours during any trading day during a draw down pricing period, that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one-eighth of the draw down amount initially specified.

The maximum number of shares of common stock that we can issue pursuant to the CEFF is 6,036,912 shares. An additional 260,000 shares of common stock are issuable if Kingsbridge exercises the warrant that we issued to it in connection with Kingsbridge s entry into the CEFF. We intend to exercise our right to draw down amounts under the CEFF, if and to the extent available, at such times as we have a need for additional capital and when we believe that sales of stock under the CEFF provide an appropriate means of raising capital.

Our ability to require Kingsbridge to purchase our common stock is subject to various limitations. We can make draw downs to a maximum of two percent of our market capitalization at the time of the draw down, or $7.0 million, whichever is less. Unless we and Kingsbridge agree otherwise, a minimum of three trading days must elapse between the expiration of any draw down pricing period and the beginning of the next succeeding draw down pricing period.

During the term of the CEFF, without the prior written consent of Kingsbridge, we may not issue securities that are, or may become, convertible or exchangeable into shares of common stock where the purchase, conversion or exchange price for that common stock is determined using any floating discount or other post-issuance adjustable discount to the market price of the common stock, including pursuant to an equity line or other financing that is substantially similar to the arrangement provided for in the CEFF.

The issuance of our common stock under the CEFF or upon exercise of the Kingsbridge warrant will have no effect on the rights or privileges of existing holders of common stock except that the economic and voting interests of each stockholder will be diluted as a result of the issuance. Although the number of shares of common stock that stockholders presently own will not decrease, these shares will represent a smaller percentage of our total shares that will be outstanding after any issuances of shares of common stock to Kingsbridge. If we draw down amounts

under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Such issuances will have a dilutive effect and may further decrease our stock price.

Kingsbridge agreed in the common stock purchase agreement that during the term of the CEFF, neither Kingsbridge nor any of its affiliates, nor any entity managed or controlled by it, will enter into any short sale of any shares of our common stock or engage, through related parties or otherwise, in any derivative transaction directly related to shares of our common stock. In addition, Kingsbridge agreed that neither Kingsbridge nor any of its affiliates, nor any entity managed or controlled by it, will sell during any draw down pricing period, shares of our common stock, other than shares of our common stock purchased (or to be purchased) during that draw down pricing period.

Before Kingsbridge is obligated to buy any shares of our common stock pursuant to a draw down, the following conditions, none of which is in the control of Kingsbridge, must be met as of the draw down exercise date and the date upon which each settlement of the purchase and sale of our common stock occurs:

Each of our representations and warranties in the common stock purchase agreement must be true and correct in all material respects as of the date when made as though made at that time, except for representations and warranties that are expressly made as of a particular date.

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We must have performed, satisfied and complied in all material respects with all covenants, agreements and conditions required by the common stock purchase agreement, the registration rights agreement and the warrant to be performed, satisfied or complied with by us.

We must have complied in all material respects with all applicable federal, state and local governmental laws, rules, regulations and ordinances in connection with the execution, delivery and performance of the common stock purchase agreement and the consummation of the transactions contemplated by it.

The registration statement, which includes this prospectus, shall have previously become effective and shall remain effective.

We shall not have knowledge of any event that could reasonably be expected to have the effect of causing the registration statement applicable to the resale of shares of our common stock by Kingsbridge to be suspended or otherwise ineffective.

Trading in our common stock shall not have been suspended by the Securities and Exchange Commission, or the SEC, the Nasdaq Stock Market or the National Association of Securities Dealers and trading in securities generally on the Nasdaq Stock Market shall not have been suspended or limited.

No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority which prohibits the consummation of any of the transactions contemplated by the common stock purchase agreement.

No action, suit or proceeding before any arbitrator or any governmental authority shall have been commenced, and no investigation by any governmental authority shall have been threatened, against us or any of our officers, directors or affiliates seeking to enjoin, prevent or change the transactions contemplated by the common stock purchase agreement.

We shall have sufficient shares of common stock, calculated using the closing trade price of the common stock as of the trading day immediately preceding a draw down, registered under the registration statement to issue and sell such shares in accordance with such draw down.

The warrant to purchase 260,000 shares of our common stock shall have been duly executed, delivered and issued to Kingsbridge, and we shall not be in default in any material aspect under the warrant.

There is no guarantee that we will be able to meet the foregoing conditions or any other conditions under the common stock purchase agreement or that we will be able to draw down any portion of the amounts available under the CEFF.

We also entered into a registration rights agreement with Kingsbridge. Pursuant to the registration rights agreement, we have filed a registration statement, which includes this prospectus, with the SEC relating to the resale by Kingsbridge of any shares of common stock purchased by Kingsbridge under the common stock purchase agreement or issued to Kingsbridge as a result of the exercise of the Kingsbridge warrant. The effectiveness of this registration statement is a condition precedent to our ability to sell common stock to Kingsbridge under the common stock purchase agreement. We are entitled in certain circumstances, including the existence of certain kinds of nonpublic information, to deliver a blackout notice to Kingsbridge to suspend the use of this prospectus and prohibit Kingsbridge from selling shares under this prospectus. If we deliver a blackout notice in the 15 trading days following a settlement of a draw down, or if the registration statement of which this prospectus is a part is not effective in circumstances not permitted by the registration rights agreement, then we must pay certain amounts to Kingsbridge (or issue Kingsbridge additional shares in lieu of payment) as liquidated damages.

The foregoing summary of the CEFF does not purport to be complete and is qualified by reference to the common stock purchase agreement, the registration rights agreement and the warrant, copies of which have been filed as exhibits to the registration statement of which this prospectus is a part.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the risk factors described below, and all other information contained in or incorporated by reference in this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations and could result in a complete loss of your investment.

Risks Related to Our Business

We are a development stage company with a limited operating history and may not be able to commercialize any products, generate revenue or attain profitability.

We are a development stage company focused on the development and commercialization of Increlex for the treatment of short stature and other endocrine disorders. From our inception in October 2000 through September 30, 2005, we have accumulated a deficit of $152.5 million. We have not generated and may not be able to generate any revenues from operations and may not be able to attain profitability. We incurred a net loss of $33.0 million during the nine months ended September 30, 2005. We expect to incur substantial net losses, in the aggregate and on a per share basis, for the foreseeable future as we attempt to develop and commercialize Increlex for severe Primary IGFD and Primary IGFD. We are unable to predict the extent of these future net losses, or when we may attain profitability, if at all. These net losses, among other things, have had and will continue to have an adverse effect on our stockholders equity and net current assets.

We anticipate that for the foreseeable future our ability to generate revenues and achieve profitability will be solely dependent on the successful commercialization of Increlex for the treatment of severe Primary IGFD and Primary IGFD. There is no assurance we will be able to obtain or maintain governmental regulatory approvals to market Increlex in the United States or rest of the world for these indications or any other indication. If we are unable to generate significant revenue from Increlex or attain profitability, we will not be able to sustain our operations.

If another company overcomes our U.S. orphan drug marketing exclusivity or obtains marketing exclusivity in Europe, it will be able to compete with us, and our revenues will be diminished.

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 FDA approval 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. Increlex has received from the FDA orphan drug marketing exclusivity for the long-term treatment of patients with severe Primary IGFD. This marketing exclusivity relates to approximately the same number of pediatric patients, and accurately describes the same pediatric patient population for which we submitted our NDA and received marketing approval. However, more than one product may be approved by the FDA for the same orphan indication or disease. As a result, even though our product has been approved and has received marketing exclusivity for severe Primary IGFD, the FDA can still approve other drugs for use in treating the same indication or disease covered by our product, which would create a more competitive market for us.

We are aware of a drug being developed by Insmed Incorporated, which we believe is a combination product containing rhIGF-1 that is in development for the treatment of severe Primary IGFD. Insmed has announced that: it has submitted an NDA for its combination product and that the FDA has determined that their drug is approvable on December 12, 2005 for the treatment of severe Primary IGFD if Insmed has met certain FDA requests. Insmed s product has received an orphan drug designation from the FDA that covers the treatment of severe Primary IGFD.

In May 2005, the FDA notified us that it considered Insmed s product to be the same drug as Increlex with respect to orphan drug marketing exclusivity. However, we may not be able to benefit from our orphan drug marketing exclusivity in the United States if the FDA determines that, with respect to orphan drug exclusivity, the two drugs are not the same. Furthermore, drugs considered to be the same as Increlex that are clinically superior or provide a major contribution to patient care may be approved for marketing by the FDA despite our initial orphan drug marketing exclusivity. If another company overcomes our U.S. orphan drug exclusivity, they will be able to compete with us, and our revenues will be diminished.

We believe that Insmed s drug has also received an orphan drug designation in Europe from the European Medicines Agency, or EMEA, that covers the treatment of severe Primary IGFD. We have not submitted a marketing authorization in Europe for severe

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Primary IGFD or any other indication. If Insmed s product is ultimately granted orphan drug marketing exclusivity for severe Primary IGFD in Europe, we may not be able to market or sell Increlex for severe Primary IGFD in Europe, and our revenues will be diminished.

If there are fewer children with severe Primary IGFD or 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 trials.

If there are fewer children with severe Primary IGFD or Primary IGFD 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 short stature is approximately one million, of which approximately 380,000 are referred to pediatric endocrinologists for evaluation. We believe that approximately 30,000 of these children have Primary IGFD, of which approximately 6,000 have severe Primary IGFD. Our estimate of the size of the patient population is based on published studies as well as internal data, including our interpretation of a study conducted as part of Genentech s National Cooperative Growth Study program. This study reported results of the evaluation of the hormonal basis of short stature in approximately 6,450 children referred to pediatric endocrinologists over a four-year period. We believe that the aggregate numbers of children in Western Europe with Primary IGFD and severe Primary IGFD are substantially equivalent to the numbers in the United States. If the results of Genentech s study or our interpretation and extrapolation of data from the study do not accurately reflect the number of children with Primary IGFD or severe Primary IGFD, our assessment of the market may be incorrect, making it difficult or impossible for us to meet our revenue goals or to enroll a sufficient number of patients in our clinical trials on a timely basis, or at all.

Increlex may fail to achieve market acceptance, which could harm our business.

rhIGF-1 has never been commercialized in the United States or Europe for any indication. Even if approved for sale by the appropriate regulatory authorities, physicians may not prescribe Increlex, in which event we may be unable to generate significant revenue or become profitable.

Acceptance of Increlex will depend on a number of factors including:

- acceptance of Increlex by physicians and patients as a safe and effective treatment;
- adequate reimbursement by third parties;
- relative convenience and ease of administration;
- prevalence and severity of side effects; and
- competitive product approvals.

Reimbursement may not be available for Increlex, which could diminish our sales and impact our ability to achieve profitability.

Market acceptance, our sales of Increlex and our profitability will depend on reimbursement policies and health care reform measures. The levels at which government authorities and third-party payors, such as private health insurers and health maintenance organizations, reimburse the price patients pay for our product will affect the commercialization of Increlex. We believe that Increlex will be reimbursed to a similar extent that growth hormone therapy is reimbursed. If our assumption regarding reimbursement for Increlex is incorrect, our expected revenues may be substantially reduced. We cannot be sure that reimbursement in the United States or elsewhere will be available for Increlex. Since the FDA approved Increlex for severe Primary IGFD, only prescriptions for that indication may be reimbursable. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, Increlex. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize Increlex.

We believe that the annual wholesale acquisition cost of Increlex therapy for the treatment of severe Primary IGFD for a 24 kilogram child would be approximately $23,000 per year. The actual cost per year per patient for Increlex will depend on the weight of the child, the treatment dose prescribed and compliance. In addition, it is possible that the children receiving Increlex therapy during the first few years of our launch are younger and/or smaller than those children receiving the drug in ensuing years, and the price per patient could be less than in subsequent years. If our assumptions regarding the price per patient of Increlex therapy for the treatment of Primary IGFD are incorrect, the market opportunity for Increlex therapy for the treatment of Primary IGFD may be substantially reduced.

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In recent years, officials have made numerous proposals to change the health care system in the United States. These proposals include measures that would limit or prohibit payments for certain medical treatments or subject the pricing of drugs to government control. In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. If our product becomes subject to government legislation that limits or prohibits payment for Increlex, or that subjects the price of our product to governmental control, we may not be able to generate revenues, attain profitability or commercialize our product. Because these initiatives are subject to substantial political debate, which we cannot predict, the trading price of biotechnology stocks, including ours, may become more volatile as this debate proceeds.

As a result of legislative proposals and the trend towards managed health care in the United States, third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which, in turn, will put pressure on the pricing of drugs.

If we do not receive additional regulatory marketing approvals of Increlex, our business will be harmed.

We are currently developing Increlex in clinical trials for the treatment of Primary IGFD, which has substantially more patients than severe Primary IGFD. The FDA has substantial discretion in the approval process and may decide that our data is insufficient to allow approval of Increlex for Primary IGFD. If we do not receive regulatory marketing approval in the United States for Primary IGFD, our business will be harmed. We will also need to file applications with regulatory authorities in foreign countries to market Increlex for Primary IGFD in foreign countries. We have not submitted a marketing authorization application in Europe for severe Primary IGFD or any other indication. If we fail to obtain European approval for Increlex, the geographic market for Increlex would be limited. If such approvals are delayed, it would postpone our ability to generate revenues in Europe.

If our contract manufacturers facilities and operations do not maintain satisfactory cGMP compliance, we may be unable to commercialize Increlex.

The facilities used by and operations of our contract manufacturers to manufacture and test Increlex must undergo continuing inspections by the FDA for compliance with cGMP regulations in order to maintain our Increlex approval. As an example, Cambrex Baltimore is our sole provider of bulk rhIGF-1. We have no alternative manufacturing facilities or plans for additional facilities at this time. We do not know if the Cambrex Baltimore facilities or their operations required for the commercial manufacture of Increlex will continue to receive satisfactory cGMP inspections. In the event these facilities or operations do not continue to receive satisfactory cGMP inspections for the manufacture of our product, or for the operation of their facilities in general, we may need to invest in significant compliance improvement programs, fund additional modifications to our manufacturing processes, conduct additional validation studies, or find alternative manufacturing facilities, any of which would result in significant cost to us as well as result in a delay or prevention of commercialization, and may result in our failure to maintain approval. In addition, Cambrex Baltimore, and any alternative contract manufacturer we may utilize, will be subject to ongoing periodic inspection by the FDA and corresponding state and foreign agencies for compliance with cGMP regulations and similar foreign standards. We do not have direct control over our contract manufacturers compliance with these regulations and standards. Any of these factors could delay or suspend clinical trials, regulatory submissions or regulatory approvals, entail higher costs and result in our being unable to effectively commercialize Increlex or maintain Increlex in the marketplace, which would adversely affect our ability to generate revenues.

We rely solely on single-source third parties in the manufacture, testing, storage and distribution of our products.

We source all of our fill-finish manufacturing and testing and final product storage and distribution operations, as well as our all of our bulk manufacturing, testing, and shipping operations, through single-source third-party suppliers and contractors. Single-source suppliers are the only approved suppliers currently available to us, and could only be replaced by qualification of new sites for the same operations.

If our contract facilities, contractors or suppliers become unavailable to us for any reason, including failure to comply with cGMP regulations, manufacturing problems or other operational failures, such as equipment failures or unplanned facility shutdowns required to comply with cGMP, damage from any event, including fire, flood, earthquake, or terrorism or if they fail to perform under our agreements with them, such as failing to deliver commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, we may be delayed in manufacturing Increlex or may be unable to maintain validation of Increlex. This could delay or prevent the supply of commercial and clinical product, or delay or otherwise adversely affect revenues. If the damage to any of these facilities is extensive, or, for any reason, they do not operate in compliance with cGMP or are unable or

refuse to perform under our licenses and/or agreements, we will need to find alternative facilities. The number of contract manufacturers with the expertise and facilities to manufacture rhIGF-1 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 expense to arrange for alternative manufacturers. If we need to change to other commercial manufacturers, these manufacturers facilities and processes, prior to our use, would likely have to undergo pre-approval and/or cGMP compliance inspections. In addition, we would need to transfer and validate the processes and analytical methods necessary for the production and testing of rhIGF-1 to these new manufacturers.

We rely in certain cases on single-source and sole-source materials suppliers to manufacture Increlex.

Certain specific components and raw materials used to manufacture Increlex at our third-party manufacturers are obtained and made available through either single-source or sole-source suppliers. Single-source suppliers are the only approved suppliers currently available to us, and could only be supplemented by qualification of new sources for the material required. Sole-source suppliers are the only source of supply available to us, and could only be replaced through qualification of an alternate material after demonstrating suitability. Supply interruption of these materials could result in a significant delay to our manufacturing schedules and ability to supply product, and would likely be required to undergo lengthy regulatory approval procedures prior to product distribution. Limits or termination of supply of these materials could significantly impact our ability to manufacture Increlex, cause significant supply delays while we qualified, at significant expense, new suppliers or new materials, and would consequently cause harm to our business.

Difficulties or delays in product manufacturing due to advance scheduling requirements and/or capacity constraints at our third-party manufacturers could harm our operating results and financial performance.

The manufacture of Increlex requires successful coordination between us and all of our suppliers, contractors, service-providers, and manufacturers. Coordination failures with these different elements of our supply chain could require us to delay shipments and/or impair our ability to supply product. Furthermore, uncertainties in estimating future demand for new products such as Increlex may result in manufacture of surplus inventory requiring us to record charges for any expired, unused product, or may result in inadequate manufacturing of product inventory, causing delays to shipments or no shipments at all. Additionally, our reliance on third-party manufacturing requires long lead times from order to delivery of product, and may be hampered by available capacity at those manufacturers, making our ability to supply product supplies in excess of our forecast extremely difficult. As a consequence, we may have inadequate capacity to meet unexpected demand, which could negatively affect our operating results.

Claims and concerns may arise regarding the safety and efficacy of Increlex, which could require us to perform additional clinical trials, could slow introduction into the marketplace, or cause reduced sales or product withdrawal after introduction.

Increlex was approved in the United States for the treatment of severe Primary IGFD based on long-term and extensive studies and clinical trials conducted to demonstrate product safety and efficacy. Discovery of previously unknown problems with the raw materials, product or manufacturing processes, such as loss of sterility, contamination, new data suggesting an unacceptable safety risk or previously unidentified side effects for the product, could result in a voluntary or mandated withdrawal of the product from the marketplace, either temporarily or permanently. Studies may result in data or evidence suggesting another product is safer, better tolerated, or more efficacious than Increlex, which could lead to reduced sales. Additionally, discovery of unknown problems with our product or manufacturing processes for our product could negatively impact the established safety and efficacy profile and result in possible reduced sales or product withdrawal. Such outcomes could negatively and materially affect our product sales, operating results, and financial condition.

We will not be able to sell our products if we are not able to maintain our regulatory approval due to changes to existing regulatory requirements.

Although we have obtained regulatory approval for Increlex in the United States for the treatment of severe Primary IGFD, this product and our manufacturing processes are subject to continued review and ongoing regulation by the FDA post approval, including, for example, changes to manufacturing process standards or good manufacturing practices, changes to product labeling, revisions to existing requirements or new requirements for manufacturing practices, or changing interpretations regarding regulatory guidance. Such changes in the regulatory environment and requirements could occur at any time during the commercialization of Increlex. This could adversely affect our ability to maintain our approval or require us to expend significant resources to maintain our approval, which could result in the possible withdrawal of Increlex from the marketplace, which would harm our business and negatively impact our financial performance.

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We face significant competition from large pharmaceutical, biotechnology and other companies that could harm our business.

The biotechnology industry is intensely competitive and characterized by rapid technological progress. In each of our potential product areas, we face significant competition from large pharmaceutical, biotechnology and other companies. Most of these companies have substantially greater capital resources, research and development staffs, facilities and experience at conducting clinical trials and obtaining regulatory approvals. In addition, many of these companies have greater experience and expertise in developing and commercializing products.

We cannot predict the relative competitive position of Increlex. However, we expect that the following factors, among others, will determine our ability to compete effectively:

safety and efficacy;

product price;

manufacturing costs;

reimbursement adoption;

ease of administration; and

marketing and sales capability.

We believe that many of our competitors spend significantly more on research and development-related activities than we do. Our competitors may discover new treatments, drugs or therapies or develop existing technologies to compete with Increlex. Our commercial opportunities will be reduced or eliminated if these competing products are more effective, have fewer or less severe side effects, are more convenient or are less expensive than Increlex.

Growth hormone will likely compete with Increlex for the treatment of patients with severe Primary IGFD and those with Primary IGFD if Increlex is approved for that indication. The major suppliers of commercially available growth hormone in the United States are Genentech, Eli Lilly and Company, Teva Pharmaceutical Industries Ltd., Novo Nordisk A/S, Pfizer Inc. and Serono S.A. Investigators from a Novo Nordisk clinical trial recently presented data that demonstrated growth hormone was effective in a population that included children with Primary IGFD. In addition, children with Primary IGFD may be diagnosed as having idiopathic short stature, or ISS, which will also cause growth hormone to be competitive with Increlex. Eli Lilly and Company and Genentech have received FDA approval for their respective growth hormone products for the treatment of children with ISS.

Insmed s combination product will compete for the treatment of patients with severe Primary IGFD if it is approved by the FDA. In addition, we are aware that Chiron Corporation has developed a process to manufacture rhIGF-1 using yeast expression and has intellectual property with respect to that process. We use bacterial expression, which differs from yeast expression, to manufacture Increlex.

In addition, we believe that Bristol-Meyers Squibb Company, Genentech, Merck & Co., Inc., Novo Nordisk and Pfizer Inc. have conducted research and development of orally available small molecules that cause the release of growth hormone, known as growth hormone secretagogues. We believe that Rejuvenon Corporation has licensed certain rights to Novo Nordisk s growth hormone secretagogues and is actively developing one of these compounds for use in cancer cachexia, a wasting disorder affecting some cancer patients.

Many companies are seeking to develop products and therapies for the treatment of diabetes. These competitors include multinational pharmaceutical companies, specialized biotechnology firms, and universities and other research institutions. Insmed has also conducted clinical trials using a product that contains rhIGF-1 for the treatment of diabetes. It is possible that there are other products currently in development or that exist on the market that may compete directly with Increlex.

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

Although we are not aware of any other company currently marketing rhIGF-1 in the United States for any 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

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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 method of use patents and/or we have orphan drug exclusivity for the use of rhIGF-1 to treat such diseases.

If we fail to protect our intellectual property rights, competitors may develop competing products, and our business will suffer.

lf we are not able to protect our proprietary technology, trade secrets and know-how, our competitors may use our inventions to develop competing products. We have licensed intellectual property rights, including patent rights, relating to rhIGF-1 technologies from Genentech. However, these patents may not protect us against our competitors. Patent litigation is very expensive, and we therefore may be unable to pursue patent litigation to its conclusion because currently we do not generate revenues.

We do not have patent composition coverage on the rhIGF-1 protein alone. Although we have licensed from Genentech its rights to its methods of use and manufacturing patents, it may be more difficult to establish infringement of such patents as compared to a patent directed to the rhIGF-1 protein composition alone. Our licensed patents may not be sufficient to prevent others from competing with us. We cannot rely solely on our patents to be successful. The standards that the U.S. Patent and Trademark Office and foreign patent offices use to grant patents, and the standards that United States and foreign courts use to interpret patents, are not the same and are not always applied predictably or uniformly and can change, particularly as new technologies develop. As such, the degree of patent protection obtained in the United States may differ substantially from that obtained in various foreign countries. In some instances, patents have issued in the United States while substantially less or no protection has been obtained in Europe or other countries. Our United States Patent No. 6,331,414 B1 licensed from Genentech is directed to methods for bacterial expression of rhIGF-1 and expires in 2018. We have no equivalent European patent. The European Patent Office has determined that the claims of Genentech s corresponding European patent application are not patentable under European patent law in view of public disclosures made before the application was filed.

We are uncertain of the level of protection, if any, that will be provided by our licensed patents if we attempt to enforce them, and they are challenged in court where our competitors may raise defenses such as invalidity, unenforceability or possession of a valid license. For example, we initiated patent infringement proceedings against Avecia Limited and Insmed Incorporated in the United Kingdom and against Insmed Incorporated in the United States to enforce patent rights we licensed from Genentech. The United States action, among other things, alleges infringement of United States Patent No. 6,311,414 B1 identified above. If the court finds any of the patents at issue in those litigations, including United States Patent No. 6,311,414 B1, to be invalid or unenforceable, we would be prevented from enforcing such patents against third parties in the future, thus preventing us from using the affected patents to exclude others from competing with us. In addition, the type and extent of patent claims that will be issued to us in the future are uncertain. Any patents that are issued may not contain claims that will permit us to stop competitors from using similar technology.

In addition to the patented technology licensed from Genentech, we also rely on unpatented technology, trade secrets and confidential information, such as the proprietary information we use to manufacture Increlex. We may not be able to effectively protect our rights to this technology or information. Other parties may independently develop substantially equivalent information and techniques or otherwise gain access to or disclose this technology. We generally require each of our employees, consultants, collaborators, and certain contractors to execute a confidentiality agreement at the commencement of an employment, consulting or collaborative relationship with us. However, these agreements may not provide effective protection of this technology or information or, in the event of unauthorized use or disclosure, they may not provide adequate remedies.

We may incur substantial costs as a result of patent infringement litigation or other proceedings relating to patent and other intellectual property rights, and we may be unable to protect our intellectual property rights.

In December 2004, we initiated patent infringement proceedings against Avecia Limited and Insmed Incorporated in the United Kingdom and against Insmed in the United States to enforce patent rights we licensed from Genentech. We cannot predict the outcome of such litigation. Either or both of those actions could require a substantial diversion of financial and personnel resources in support of such actions and expose us to liability for costs or other awards of damages. Declaratory judgments of invalidity against our patents asserted in such actions could prevent us from using the affected patents to exclude others from competing with us.

In addition, a third party may claim that we are using its inventions covered by its patents and may initiate litigation to stop us from engaging in our operations and activities. Although no third party has claimed that we are infringing on their patents, patent lawsuits are costly and could affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we are infringing the third party s patents and would order us to stop the activities covered by the patents. In addition, there is a risk that a court will order us to pay the other party damages for having infringed the other party s

patents. The biotechnology industry has produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our products or methods of use do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid, and we may not be able to do so. Proving invalidity, in particular, is difficult since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents.

We are aware of a U.S. patent of Chiron Corporation related to processes of manufacturing rhIGF-1 in yeast host cells, to fusion proteins, DNA, and yeast host cells useful in such processes of manufacturing rhIGF-1 in yeast host cells, and to rhIGF-1 made as a product of such processes. While we use bacterial expression, not yeast expression, in our process for manufacturing Increlex, we cannot predict whether our activities relating to the development and commercialization of Increlex in the United States will be found to infringe Chiron s patent in the event Chiron brings patent infringement proceedings against us. We may not be able to obtain a license to Chiron s patent under commercially reasonable terms, if at all. If we are unable to obtain a license to Chiron s patent, and if in any patent infringement proceeding Chiron brings against us the court decides that our activities relating to the development and commercialization of Increlex in the United States infringe Chiron s patent, the court may award damages and/or injunctive relief to Chiron. Any such damages, injunctive relief and/or other remedies the court may award could render any further development and commercialization of Increlex commercially infeasible for us or otherwise curtail or cease any further development and commercialization of Increlex.

We cannot be certain that others have not filed patent applications for technology covered by our licensor s issued patents or our pending applications or our licensor s pending applications or that we or our licensors were the first to invent the technology because:

- some patent applications in the United States may be maintained in secrecy until the patents are issued,
- patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and
- publications in the scientific literature often lag behind actual discoveries and the filing of patents relating to those discoveries.

Patent applications may have been filed and may be filed in the future covering technology similar to ours. Any such patent application may have priority over our patent applications and could further require us to obtain rights to issued patents covering such technologies. In the event that another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the U.S. Patent and Trademark Office to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our United States patent position with respect to such inventions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could harm our business.

If we lose our licenses from Genentech, we may be unable to continue our business.

We have licensed intellectual property rights and technology from Genentech, under our U.S. and International License and Collaboration agreements with Genentech. Under each agreement, Genentech has the right to terminate our license if we are in material breach of our obligations under that agreement and fail to cure that breach. Under the terms of the agreements, we are obligated, among other things, to use reasonable business efforts to meet specified milestones, including filing for regulatory approval in the United States for an IGFD indication by December 31, 2005, which we have accomplished, and for either a diabetes indication or a substitute indication by December 31, 2008. Additionally, we are obligated to file for regulatory approval in either the European Union or Japan for an IGFD indication by December 31, 2007. If we fail to use reasonable business efforts to meet our development milestones for either agreement, Genentech may terminate that agreement. If either agreement were terminated, then we would lose our rights to utilize the technology and intellectual property covered by that agreement to develop, manufacture and commercialize Increlex for any indication. This may prevent us from continuing our business.

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We are subject to Genentech s option rights with respect to the commercialization of Increlex for all diabetes and non-orphan indications in the United States.

Under our U.S. License and Collaboration Agreement with Genentech, Genentech has the option to elect to jointly commercialize rhIGF-1 for all diabetes and non-orphan indications in the United States. Orphan indications are designated by the FDA under the Orphan Drug Act, and are generally rare diseases or conditions that affect fewer than 200,000 individuals in the United States. With respect to those non-orphan and diabetes indications in the United States, once Genentech has exercised its option to jointly develop and commercialize, Genentech has the final decision on disputes relating to development and commercialization of such indications. Our ability to sublicense the development and commercialization of such products requires the consent of Genentech.

We do not know whether our planned clinical trials will begin on time, or at all, or will be completed on schedule, or at all.

The commencement or completion of any of our clinical trials may be delayed or halted for numerous reasons, including, but not limited to, the following:

- the FDA or other regulatory authorities either do not approve a clinical trial protocol or place a clinical trial on clinical hold;
- patients do not enroll in clinical trials at the rate we expect (e.g., in one of our current Phase III clinical trials of rhIGF-1 in Primary IGFD, patients have not enrolled at the rate we expected);
- patients experience adverse side effects;
- patients develop medical problems that are not related to our products or product candidates;
- third-party clinical investigators do not perform our clinical trials on our anticipated schedule or consistent with the clinical trial protocol and good clinical practices, or other third-party organizations do not perform data collection and analysis in a timely or accurate manner;
- contract laboratories fail to follow good laboratory practices;
- interim results of the clinical trial are inconclusive or negative;
- sufficient quantities of the trial drug may not be available, or available drug may become unusable;
- our trial design, although approved, is inadequate to demonstrate safety and/or efficacy;
- re-evaluation of our corporate strategies and priorities; and

limited financial resources.

In addition, we may choose to cancel, change or delay certain planned clinical trials, or replace one or more planned clinical trials with alternative clinical trials. Our clinical trials or intended clinical trials may be subject to further change from time to time as we evaluate our research and development priorities and available resources. Our development costs will increase if we need to perform more or larger clinical trials than planned. Significant delays for our current or planned clinical trials may harm the commercial prospects for Increlex and our prospects for profitability.

Clinical development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials.

To gain approval to market a product for treatment of a specific disease, we must provide the FDA and foreign regulatory authorities with clinical data that demonstrate the safety and statistically significant efficacy of that product for the treatment of the disease. Clinical development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. If a clinical trial failed to demonstrate safety and statistically significant efficacy, we would likely abandon the development of that product, which could harm our business and may result in a precipitous decline in our stock price.

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If third-party clinical research organizations do not perform in an acceptable and timely manner, our clinical trials could be delayed or unsuccessful.

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

We may need others to market and commercialize Increlex in Europe.

We may need others to market and commercialize Increlex in Europe. If we decide to sell Increlex in Europe through a third party, we will need to enter into marketing arrangements with them. We may not be able to enter into marketing arrangements with third parties on favorable terms, or at all. In addition, these arrangements could result in lower levels of income to us than if we marketed Increlex entirely on our own. In the event that we are unable to enter into a marketing arrangement for Increlex in Europe, we may not be able to develop an effective sales force to successfully commercialize our product in Europe. If we fail to enter into marketing arrangements for our product and are unable to develop an effective international sales force, our revenues could be limited.

If we fail to identify and in-license other patent rights, products or product candidates, we may be unable to grow our revenues.

We do not conduct any preclinical laboratory research. Our strategy is to in-license products or product candidates and further develop them for commercialization. The market for acquiring and in-licensing patent rights, products and product candidates is intensely competitive. If we are not successful in identifying and in-licensing other patent rights, products or product candidates, we may be unable to grow our revenues with sales from new products.

In addition, we may need additional intellectual property from other third parties to commercialize Increlex for indications other than severe Primary IGFD or Primary IGFD. We cannot be certain that we will be able to obtain a license to any third-party technology we may require to conduct our business.

If we fail to obtain the capital necessary to fund our operations, we will be unable to execute our business plan.

We believe that our cash, cash equivalents and short-term investments as of September 30, 2005 of $71.0 million and the proceeds available under our senior credit facility and the CEFF will be sufficient to meet our projected operating and capital expenditure requirements through at least the end of 2006 based on our current business plan. We expect capital outlays and operating expenditures to increase over the next several years as we expand our operations.

Our future capital needs and the adequacy of our available funds will depend on many factors, including:

our ability to market and sell sufficient quantities of rhIGF-1;

the costs, timing and scope of additional domestic and international regulatory approvals for rhIGF-1;

the status of competing products;