CELL THERAPEUTICS INC
Form S-3
December 16, 2005
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As filed with the Securities and Exchange Commission on December 16, 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

CELL THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Washington	**2834**	**91-1533912**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification Number)**

501 Elliott Avenue West, Suite 400

Seattle, Washington 98119

(206) 282-7100

(Address, including zip code, and telephone number, including area code, of Registrant s principal executive offices)

James A. Bianco

President and Chief Executive Officer

Cell Therapeutics, Inc.

501 Elliott Avenue West, Suite 400

Seattle, Washington 98119

(206) 282-7100

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Michael J. Kennedy, Esq.

O Melveny & Myers LLP

Embarcadero Center West

275 Battery Street, Suite 2600

San Francisco, California 94111-3305

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 (hereinafter the Securities Act), 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, please 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	Proposed Maximum Offering Price Per Security(2)	Aggregate Offering Price	Amount of Registration Fee
$82,000,000 6.75% Convertible Senior Notes due October 31, 2010	$82,000,000(1)	100%	$82,000,000	$8,774
Common Stock, no par value per share(3)	31,540,340(4)	$2.31(4)	$808,500(4)	$87(5)(6)

(1) Represents the aggregate principal amount of the notes issued by the Registrant.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933 and exclusive of accrued interest and distributions, if any.

(3) Shares of the registrant s common stock being registered hereby are accompanied by the registrant s preferred stock purchase rights. Until the occurrence of certain prescribed events, such rights are not exercisable, are evidenced by each certificate for common stock and will be transferred along with and only with the common stock.

(4) Represents (i) 31,190,340 shares of common stock issuable upon conversion of the notes at the conversion rate of 380.37 shares per each $1,000 principal amount of notes, subject to adjustment in certain circumstances, which is equivalent to an initial conversion price of approximately $2.63 per share of common stock. Pursuant to Rule 416 under the Securities Act, such number of shares of common stock registered hereby shall include an indeterminate number of shares of common stock that may be issued in connection with a stock split, stock dividend, recapitalization or similar event, and (ii) 350,000 shares of common stock issuable upon the exercise of warrants with an exercise price of $3.50 per share.

(5) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act, based on the average of the high and low prices for the registrant s common stock as reported on the Nasdaq National Market on December 15, 2005, which was $2.31.

(6) Pursuant to Rule 457(i), no additional filing fee is payable with respect to the shares of common stock issuable upon conversion of the notes because no additional consideration will be received in connection with the exercise of the conversion privilege.

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 which 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 Commission, acting pursuant to said Section 8(a), may determine.

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

Subject to Completion,

Dated December 16, 2005

PRELIMINARY PROSPECTUS

Making cancer more treatable™

$82,000,000

6.75% Convertible Senior Notes due October 31, 2010

and the common stock issuable upon conversion of the notes

We issued the notes offered by this prospectus in a private placement in November 2005. This prospectus will be used by selling securityholders to resell their notes and the common stock issuable upon conversion of their notes and the exercise of warrants. We will not receive any proceeds from this offering.

You may convert the notes into shares of our common stock at any time before their maturity unless we have previously redeemed or repurchased them. The notes will be due on October 31, 2010. The conversion rate is 380.37 shares per each $1,000 principal amount of notes, subject to adjustment in certain circumstances. This is equivalent to an initial conversion price of approximately $2.63 per share.

We will pay interest on the notes on April 30 and October 31 of each year. The first interest payment will be made on April 30, 2006. The notes will be senior in right of payment to our 5.75% Convertible Subordinated Notes due 2008, our 5.75% Convertible Senior Subordinated Notes due 2008 and our 4% Convertible Senior Subordinated Notes due 2010.

On April 30, 2006, you shall have the right to cause us to redeem in cash up to 30% of the aggregate principal amount of the notes on a pro rata basis. Such redemption will be at par, but excluding accrued and unpaid interest through the redemption date. Any such interest not paid upon redemption will be forfeited to us. We shall hold in escrow, out of the net proceeds of the initial offering, an amount equal to the aggregate

amount necessary to fund any such redemptions.

The notes are not listed on any securities exchange or included in any automated quotation system. The notes are eligible for trading in the PORTAL[SM] Market of the National Association of Securities Dealers, Inc. Our common stock is quoted on the Nasdaq National Market under the symbol CTIC. On December 15, 2005, the last reported sale price for our common stock on the Nasdaq National Market was $2.29 per share.

Investing in the notes involves risk. See **Risk Factors** beginning on page 7.

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.

This prospectus is dated , 2005

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PROSPECTUS SUMMARY

The following is a summary of this prospectus. The following summary does not contain all the information that you should consider before investing in the notes. You should read this entire prospectus carefully, including the documents that we have incorporated by reference into this prospectus. Unless otherwise indicated, CTI, Company, we, us, our and similar terms refer to Cell Therapeutics, Inc. and its subsidiaries.

Our Company

We develop, acquire and commercialize novel treatments for cancer. Our goal is to build a leading biopharmaceutical company with a diversified portfolio of proprietary oncology drugs. Our research, development, acquisition and in-licensing activities concentrate on identifying and developing new, less toxic and more effective ways to treat cancer. We are developing XYOTAX, paclitaxel poliglumex, for the treatment of non-small cell lung cancer, or NSCLC, and ovarian cancer. Our phase III clinical studies for XYOTAX did not meet our primary endpoint of superior overall survival. However, in a pooled analysis of our STELLAR 3 and 4 pivotal trials, woman receiving XYOTAX for first-line treatment of NSCLC had statistically significant improvement in median, 1 year and overall survival compared to women receiving standard first-line chemotherapy. In addition, a phase II clinical trial that we reported in September 2005 demonstrated a survival advantage for women receiving XYOTAX as first-line therapy for NSCLC when compared to men. We, therefore, plan to submit a new drug application, or NDA, with the U.S. Food and Drug Administration, or FDA, for XYOTAX as first-line monotherapy for women with advanced NSCLC who have poor performance status (PS2) based on data from the pooled analysis of our STELLAR 3 and 4 first-line trials. To support this indication, we also have initiated an additional study for XYOTAX as first-line monotherapy in women and to have interim results available at the time of FDA review of that NDA, as an alternative to waiting for the completion of the study. In Europe, we plan to submit a marketing authorization application, or MAA, based on non inferior survival and improved side effect profile demonstrated in our first-line pivotal trials. We will need additional positive input from the Scientific Advisory Working Group of the European Medicines Agency, or EMEA, prior to submitting an MAA on these bases. We are developing pixantrone, a novel anthracycline derivative, for the treatment of non-Hodgkin s lymphoma, or NHL. We are targeting an interim analysis from our ongoing phase III study late in the second quarter of 2006. We also are developing CT-2106, polyglutamate camptothecin, which is in a phase I/II trial for the treatment of colorectal cancer and a phase II trial in ovarian cancer. In the first half of 2005, we commenced a cost savings initiative, including a reduction of workforce, in an effort to conserve capital.

We were incorporated in Washington in 1991. Our principal office is located at 501 Elliott Avenue West, Suite 400, Seattle, WA 98119. Our telephone number is (206) 282-7100. Our world wide web address is *http://www.cticseattle.com*. Information on our website does not constitute part of this prospectus. CTI and XYOTAX (formerly referred to as PG-TXL) are our proprietary marks. All other product names, trademarks and trade names referred to in this prospectus are the property of their respective owners.

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The Offering

The following is a brief summary of some of the terms of the notes offered for resale in this prospectus. For a more complete description of the terms of the notes, see the Description of Notes section in this prospectus.

Securities Offered	$82,000,000 aggregate principal amount of 6.75% Convertible Senior Notes due October 31, 2010.
Mandatory Redemption Right	On April 30, 2006, you shall have the right to cause us to redeem in cash up to 30% of the aggregate principal amount of the notes on a pro rata basis. Such redemption will be at par and will exclude any accrued and unpaid interest through the redemption date. Any such interest not paid to you upon redemption will be forfeited to us. We shall hold in escrow, out of the net proceeds of this offering, an amount equal to the aggregate amount necessary to fund any such redemptions.
Issuer	Cell Therapeutics, Inc.
Maturity	October 31, 2010
Offering Price	100% of the principal amount.
Interest	Interest is payable on the notes at a rate of 6.75% per year, payable in cash, registered common stock or some combination of cash and registered common stock having a fair market value equal to the interest payment due, semi-annually on April 30 and October 31 of each year, beginning April 30, 2006. For the purposes of this provision, the fair market value of our common stock shall be equal to 95% of its volume-weighted average price for the five consecutive trading days ending on the trading day immediately preceding the interest payment date.
Conversion	You have the option to convert the notes into shares of our common stock at a conversion rate of 380.37 shares of common stock per $1,000 principal amount of our notes, which is equivalent to a conversion price of approximately $2.63 per share. The conversion rate is subject to adjustment as described more fully in the Description of the Notes Conversion Rights. You may convert the notes at any time before the close of business on the maturity date, unless we have previously redeemed or repurchased our notes; provided, however, that if a note is called for repurchase, you will be entitled to convert the note at any time before the close of business on the date immediately preceding the date fixed for repurchase. See Description of Notes Conversion Rights.
Optional Redemption	We have the option to redeem all, but not less than all, of the notes if the closing price per share of our common stock has exceeded 125% of the conversion price then in effect for at least 20 trading days within any 30-consecutive trading day period, provided that for each day during such 30 trading day period a shelf registration statement was in effect with respect to the resale of the shares of our common stock underlying these notes. The redemption price shall be par including accrued and unpaid interest up to but not including the redemption date and shall be payable in shares of registered common stock valued at the conversion price then in effect. See Description of Notes Conversion Rights.

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Make-Whole Provision	Upon any conversion of the notes, we will pay to you an amount equal to $337.50 per $1,000 principal amount of your notes so converted, less the amount of any interest paid on such notes prior to the conversion date. This payment may be made in cash, registered common stock or some combination of cash and registered common stock. For the purposes of this provision, the fair market value of our common stock shall be equal to 95% of its volume-weighted average price for the five consecutive trading days ending on the trading day immediately preceding the conversion date.
Ranking	The notes rank *pari passu* in right of payment with all existing and future senior indebtedness. The notes are senior to our existing 5.75% Convertible Subordinated Notes due 2008, our 5.75% Convertible Senior Subordinated Notes due 2008 and our 4% Convertible Senior Subordinated Notes due 2010. The notes are structurally subordinated in right of payment to the liabilities of our subsidiaries. The indenture governing the notes restricts our incurrence of indebtedness and our subsidiaries incurrence of indebtedness. See Description of Notes Ranking.
Repurchase at Option of Holders Upon a Change in Control	Upon a change in control (as defined in the indenture), you will have the right, subject to various conditions and restrictions, to require us to repurchase your notes, in whole or in part, at 100% of their principal amount, plus accrued and unpaid interest to, but excluding, the repurchase date. The repurchase price is payable, at our option, in cash, in shares of registered common stock or a combination of cash and registered common stock. However, we, or the successor entity in the change in control transaction, may pay the repurchase price in common stock only if the conditions provided in the indenture governing the notes are satisfied. If the repurchase price is paid in common stock, the common stock will be valued at 95% of the average of the volume weighted average price per share of our common stock for each of the five consecutive trading days ending on the trading day immediately preceding the repurchase date. A change in control could be an event of default under our senior debt. See Description of Notes Repurchase at Option of Holders Upon a Change in Control.
Use of Proceeds	We will not receive any proceeds from the sale by any selling securityholder of the notes or the shares offered by this prospectus.
Covenants	We have agreed not to incur or suffer to exist, and to not permit our subsidiaries to incur or suffer to exist (i) any indebtedness that is structurally senior or senior by its terms to these notes, or (ii) secured indebtedness, in an aggregate principal amount for both clauses (i) and (ii) exceeding $10,000,000 unless, in the case of clause (ii) only, these notes are equally and ratably secured with such secured indebtedness, except that we may incur liens or encumbrances in connection with biopharmaceutical licensing and/or partnering arrangements.

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	We have also agreed (i) not to issue any preferred equity or debt security convertible into or exchangeable for our common stock and (ii) not to refinance, retire or exchange any of our existing 5.75% Convertible Subordinated Notes due 2008, 5.75% Convertible Senior Subordinated Notes due 2008 or 4% Convertible Senior Subordinated Notes due 2010 prior to March 31, 2006, subject to certain exceptions. After this date, if we refinance, retire or exchange our existing 5.75% Convertible Subordinated Notes due 2008, 5.75% Convertible Senior Subordinated Notes due 2008 or 4% Convertible Senior Subordinated Notes due 2010 by issuing new indebtedness, we agree that such newly issued indebtedness will have a maturity date later than the maturity date of these notes.
Blocker Provision	We will not (i) effect any conversion of any of these notes, and you will not have the right to convert any portion of these notes, or (ii) make any interest payment or make-whole payment in shares of our common stock in respect of any of these notes, in either case to the extent that after giving effect to such conversion or payment you would beneficially own 9.5% or more of the number of shares of our common stock outstanding immediately after giving effect to such conversion or payment. To the extent that this blocker provision prevents us from issuing to you sufficient shares of our common stock to satisfy in full any conversion or interest or make-whole payment obligation, we shall issue to you a number of zero strike price warrants equal to the number of shares of our common stock that we are precluded by the terms of this blocker provision from issuing to you. Such zero strike price warrants shall have an expiration date of October 31, 2010 and will themselves contain provisions similar to this blocker provision.
Events of Default	The following will be events of default under the indenture for the notes:
	we fail to pay the principal of or any premium on the notes when due, whether or not the payment is prohibited by the indenture s subordination provisions;
	we fail to pay any interest on the notes when due and that default continues for 30 days, whether or not the payment is prohibited by the indenture s subordination provisions;
	we fail to give the notice that we are required to give if there is a change in control, whether or not the notice is prohibited by the indenture s subordination provisions;
	we fail to perform any other covenant in the indenture and that failure continues for 60 days after written notice to us by the trustee or the holders of at least 25% in aggregate principal amount of outstanding notes;
	we fail to pay when due the principal of any indebtedness for money borrowed by us or any of our subsidiaries in excess of $10 million if the indebtedness is not discharged and such failure continues for 30 days or more, or, if such indebtedness has been accelerated and such acceleration is not annulled, within 30 days after written notice to us by the trustee or the holders of at least 25% in aggregate principal amount of the outstanding notes; and

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	certain events of bankruptcy, insolvency or reorganization with respect to Cell Therapeutics, Inc. and its significant subsidiaries specified in the indenture
	See Description of Notes Events of Default.
Nasdaq National Market Symbol for Our Common Stock	CTIC

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Risk Factors

You should read the Risk Factors section, beginning on page 7 of this prospectus, so that you understand the risks associated with an investment in the notes.

RATIO OF EARNINGS TO FIXED CHARGES

The ratio of earnings to fixed charges for each of the periods indicated is as follows:

	Year Ended December 31,					Nine Months Ended September 30,	
	2000	2001	2002	2003	2004	2004	2005
Ratio of earnings to fixed charges(1)							

(1) For the purposes of computing ratio of earnings to fixed charges, earnings consist of income (loss) before provision for income taxes plus fixed charges. Fixed charges consist of interest charges and that portion of rental payments under operating leases we believe to be representative of interest. Earnings for the years ended December 31, 2000, 2001, 2002, 2003, 2004, and for the nine months ended September 30, 2004 and 2005, were insufficient to cover fixed charges by $51,929, $80,273, $49,903, $130,031, $252,298, $208,761 and $83,811 (in thousands) respectively.

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RISK FACTORS

You should carefully consider the risks described below and other information in this prospectus and in the documents incorporated by reference into this prospectus before deciding to invest in the notes or the common stock issuable upon conversion of the notes.

The risks and uncertainties described below are not the only ones facing our company. Additional risks and uncertainties that we do not presently know or that we currently deem immaterial may also impair our business, financial condition, operating results and prospects.

If any of the following risks actually occur, they could materially adversely affect our business, financial condition, operating results or prospects. In that case, the trading price of our securities could decline.

Risks Related To Our Business

We expect to continue to incur net losses, and we might never achieve profitability.

We were incorporated in 1991 and have incurred a net operating loss every year. As of September 30, 2005, we had an accumulated deficit of approximately $806.6 million. Effective July 18, 2005, we divested our sole commercial product TRISENOX® (arsenic trioxide) and we may never become profitable, even if we are able to commercialize other products. We are pursuing regulatory approval for XYOTAX and will need to conduct research, development, testing and regulatory compliance activities expenses for which, together with projected general and administrative expenses, will result in operating losses for the foreseeable future.

We expect to need to raise additional funds in the near future, and they may not be available on acceptable terms, or at all.

As of September 30, 2005, we expected that our existing capital resources, including the proceeds from our November 2005 convertible senior notes offering, net of amounts held in escrow until April 30, 2006 to fund potential mandatory redemptions of these notes, and our ability to control expenditures would enable us to maintain our operations for at least the next twelve months based on then current activities; however, to fully fund ongoing and planned activities beyond the next twelve months, we will need to raise additional funds. In particular, we will need to raise additional funds to complete an additional study for XYOTAX as first-line monotherapy in women and the regulatory approval process for XYOTAX.

If our plans or assumptions change or are inaccurate, it will affect the amount of additional funds we will need to raise. We may raise such capital through public or private equity financings, partnerships, debt financings or restructurings, bank borrowings or other sources. Additional funding may not be available on favorable terms or at all. If adequate funds are not otherwise available, we will further curtail operations significantly, including the delay, modification or cancellation of operations and plans related to XYOTAX, pixantrone and other products we may be developing. To obtain additional funding, we may need to enter into arrangements that require us to relinquish rights to certain technologies, drug candidates, products and/or potential markets. To the extent that additional capital is raised through the sale of equity, or securities convertible into equity, shareholders may experience dilution of their proportionate ownership of us.

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The terms of our newly issued 6.75% convertible senior notes and the terms of the related Conversion and Placement Agreement preclude us from pursuing certain financings for various periods of time, and if one or more of the resale registration statements that we have agreed to file is not declared effective, we may be precluded from raising funds through equity or debt financings for an extended period of time.

We may be delayed, limited or precluded from obtaining regulatory approval of XYOTAX given that each of our three STELLAR phase III clinical trials for the treatment of non-small cell lung cancer did not meet their primary endpoints.

In March 2005, we announced the results of STELLAR 3, and in May 2005, we announced the results of STELLAR 2 and 4, our phase III clinical trials of XYOTAX in non-small cell lung cancer. All three trials, which were designed to demonstrate a significant improvement in overall survival compared to current marketed agents for treating NSCLC, did not achieve their primary endpoints of superior overall survival. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval. Negative or inconclusive results or adverse medical events during a clinical trial could delay, limit or prevent regulatory approval. Our success depends in large part on obtaining regulatory approval of XYOTAX. Our filing strategy for XYOTAX has not been previewed or approved by the FDA, the EMEA or any other regulatory authority, and we expect that obtaining regulatory approval based on our current clinical trial data will be difficult as described below.

Without a successful additional trial or positive interim results from that additional trial, we expect a difficult regulatory review from the FDA, which may preclude obtaining approval of our new drug application, or NDA, for a number of reasons: our trials failed to meet their primary endpoints and the FDA has taken the view that it will not favorably review secondary endpoints on data absent achievement of primary endpoints; while gender-specific survival was pre-specified in the analysis plan, women over men gender-specific survival was not a pre-specified endpoint; and, while the FDA has recently reviewed NDAs based on pooled analyses, none have been approved in the past. We are not pursuing approval from the FDA based on non-inferiority which is usually the basis for making a comparable survival claim.

A successful regulatory review from the EMEA is also not assured. While one EMEA member country supported using a non-inferiority overall survival endpoint for each of the STELLAR first-line studies, the EMEA Scientific Advisory Working Group will need to agree on the statistical tests and methodologies used to support this non-inferiority endpoint. The EMEA Scientific Advisory Working Group may not reach such an agreement and may not support submission to the EMEA for review and potential approval.

We have a substantial amount of debt.

We have outstanding over $233 million of debt as of November 30, 2005. Over $96 million of this debt comes due in 2008 and over $137 million comes due in 2010. Assuming the mandatory redemption right for the notes is not exercised, our annual interest expense, including the interest payable pursuant to the 6.75% convertible senior notes, will be over $13 million. Unless we generate substantial sales from one of our potential products or raise substantial additional capital, we may not be able to repay this debt or the interest, liquidated damages or other payments with respect to our debt. Prior to this debt becoming due, we may engage in one or more restructuring transactions which could involve, among other things, an effective increase in interest rates, alteration of terms or exchanges involving the issuance of additional shares of common stock or other arrangements which may dilute or be adverse to the value of our common stock.

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We are subject to extensive government regulation.

We are subject to rigorous and extensive regulation by the FDA in the United States and by comparable agencies in other countries. Failure to comply with regulatory requirements could result in various adverse consequences, including possible delay in approval or refusal to approve a product, withdrawal of approved products from the market, product seizures, injunctions, monetary penalties, or criminal prosecution.

Our products may not be marketed in the United States until they have been approved by the FDA and may not be marketed in other countries until they have received approval from the appropriate agency. With the exception of TRISENOX, which we recently divested to Cephalon, Inc., or Cephalon, none of our products have received approval. Obtaining regulatory approval requires substantial time, effort and financial resources, and we may not be able to obtain approval of any of our products on a timely basis, or at all. If our products are not approved in a timely fashion, our business and financial condition may be adversely affected.

The next product for which we expect to request approval is XYOTAX. We intend to request that the FDA approve XYOTAX as first-line monotherapy for women with advanced NSCLC who have poor performance status (PS2) based on data from a pooled analysis of two trials. We also plan to initiate an additional study of XYOTAX as first-line monotherapy in women and to have interim results available at the time of FDA review. Based on feedback from the FDA, we expect that it will be difficult to obtain approval based on the data available from our existing trials, and we cannot be sure that XYOTAX will be approved based on this submission or on any other submission in the future.

In addition, both before and after approval, our contract manufacturers and our products are subject to numerous FDA requirements covering, among other things, testing, manufacturing, quality control, labeling, advertising, promotion, distribution and export. Manufacturing processes must conform to current Good Manufacturing Practice, or cGMPs. The FDA and other regulatory authorities periodically inspect manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort to maintain compliance.

We believe that while we owned TRISENOX, it was prescribed by physicians largely for uses not approved by the FDA. Although physicians may lawfully prescribe pharmaceutical products, such as TRISENOX, for such off-label uses, promotion by us of such off-label uses is unlawful. Some of our practices intended to make physicians aware of off-label uses of TRISENOX, without engaging in off-label promotion, could nevertheless have been construed as off-label promotion, and it is likely that some instances of off-label promotion occurred in the past. We are in discussions with the U.S. Attorney for the Western District of Washington in connection with previous promotional practices. Although we have policies and procedures in place designed to assure ongoing compliance with FDA requirements regarding off-label promotion, some non-compliant actions may nevertheless have occurred. Regulatory authorities could take enforcement action against us if they believe that we promoted TRISENOX for off-label use.

Additionally, we are subject to numerous regulations and statutes regulating the manner of selling and obtaining reimbursement for our products that receive marketing approval. For example, federal statutes generally prohibit providing certain discounts and payments to physicians to encourage them to prescribe our product. Violations of such regulations or statutes may result in treble damages, criminal or civil penalties, fines or exclusion of CTI or our employees from participation in federal and state healthcare programs. Although we have policies prohibiting violations of relevant regulations and statutes, unauthorized actions of our employees or consultants (including unlawful off-label promotion),

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or unfavorable interpretations of such regulations or statutes may result in third-parties or regulatory agencies bringing legal proceedings or enforcement actions against us.

We face direct and intense competition from our competitors in the biotechnology and pharmaceutical industries, and we may not compete successfully against them.

Competition in the oncology industry is intense and is accentuated by the rapid pace of technological development. We anticipate that we will face increased competition in the future as new companies enter our market. Our competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions. Specifically:

If we are successful in bringing XYOTAX to market, we will face direct competition from oncology-focused multinational corporations. XYOTAX will compete with other taxanes. Many oncology-focused multinational corporations currently market or are developing taxanes, epothilones, and other cytotoxic agents, which inhibit cancer cells by a mechanism similar to taxanes, or similar products including, among others, Bristol-Myers Squibb Co., which markets paclitaxel; Aventis, which markets docetaxel; Genentech and OSI Pharmaceuticals, which market Tarceva ; Genentech, which markets Avastin , Lilly, which markets Alimta®; and American Pharmaceutical Partners, which markets Abraxane . In addition, several companies such as NeoPharm Inc. and Sonus Pharmaceuticals, are also developing novel taxanes and formulations which could compete with our products.

Because pixantrone is intended to provide less toxic treatment to patients who have failed standard chemotherapy treatment, if pixantrone is brought to market, it is not expected to compete directly with many existing chemotherapies. However, pixantrone will face competition from currently marketed anthracyclines, such as mitoxantrone (Novantrone®), and new anti-cancer drugs with reduced toxicity that may be developed and marketed.

Many of our competitors, either alone or together with their collaborators and in particular, the multinational pharmaceutical companies, have substantially greater financial resources and development and marketing teams than us. In addition, many of our competitors, either alone or together with their collaborators, have significantly greater experience than we do in developing, manufacturing and marketing products. As a result, these companies products might come to market sooner or might prove to be more effective, less expensive, have fewer side effects or to be easier to administer than ours. In any such case, sales of our products or eventual products would likely suffer and we might never recoup the significant investments we are making to develop these product candidates.

Uncertainty regarding third-party reimbursement and healthcare cost containment initiatives may limit our returns.

The ongoing efforts of governmental and third-party payors to contain or reduce the cost of healthcare may affect our ability to commercialize our products successfully. Governmental and other third-party payors are increasingly attempting to contain healthcare costs by:

challenging the prices charged for health care products and services,

limiting both coverage and the amount of reimbursement for new therapeutic products,

denying or limiting coverage for products that are approved by the FDA but are considered experimental or investigational by third-party payors,

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refusing in some cases to provide coverage when an approved product is used for disease indications in a way that has not received FDA marketing approval, and

denying coverage altogether.

The trend toward managed healthcare in the United States, the growth of organizations such as health maintenance organizations, and legislative proposals to reform healthcare and government insurance programs could significantly influence the purchase of healthcare services and products, resulting in lower prices and reducing demand for our products. In addition, in almost all European markets, pricing and choice of prescription pharmaceuticals are subject to governmental control. Therefore, the price of our products and their reimbursement in Europe will be determined by national regulatory authorities.

Even if we succeed in bringing any of our proposed products to the market, they may not be considered cost-effective and third-party reimbursement might not be available or sufficient. If adequate third-party coverage is not available, we may not be able to maintain price levels sufficient to realize an appropriate return on our investment in research and product development. In addition, legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us before or after any of our proposed products are approved for marketing. The Medicare Prescription Drug Improvement, and Modernization Act, or MMA, enacted December 2003, will affect reimbursement and purchases of prescription drugs, including cancer drugs. Implementation of the MMA and yet to be issued regulation could have an adverse impact on sales of prescription drugs. While we cannot predict whether any other legislative or regulatory proposals will be adopted, the adoption of other proposals could make it difficult or impossible to sell our products.

Even if our drug candidates are successful in clinical trials, we may not be able to successfully commercialize them.

Since our inception in 1991, we have dedicated substantially all of our resources to the research and development of our technologies and related compounds. With the exception of TRISENOX for patients with acute promyelocytic leukemia, or APL, who have relapsed or failed standard therapies, which we recently divested to Cephalon, all of our compounds currently are in research or development, and none have been submitted for marketing approval.

Prior to commercialization, each product candidate requires significant additional research, development and preclinical testing and extensive clinical investigation before submission of any regulatory application for marketing approval. The development of anti-cancer drugs, including those we are currently developing, is unpredictable and subject to numerous risks. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons including that they may:

be found ineffective or cause harmful side effects during preclinical testing or clinical trials,

fail to receive necessary regulatory approvals,

be difficult to manufacture on a scale necessary for commercialization,

be uneconomical to produce,

fail to achieve market acceptance, or

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be precluded from commercialization by proprietary rights of third parties.

The occurrence of any of these events could adversely affect the commercialization of our products. Products, if introduced, may not be successfully marketed and/or may not achieve customer acceptance. If we fail to commercialize products or if our future products do not achieve significant market acceptance, we will not likely generate significant revenues or become profitable.

If any of our license agreements for intellectual property underlying XYOTAX, pixantrone or any other products are terminated, we may lose our rights to develop or market that product.

We have licensed intellectual property, including patent applications from The University of Vermont, Hoffman La Roche and others, including the intellectual property relating to pixantrone. We have also in-licensed the intellectual property relating to our drug delivery technology that uses polymers that are linked to drugs, known as polymer-drug conjugates, including XYOTAX and CT-2106. Some of our product development programs depend on our ability to maintain rights under these licenses. Each licensor has the power to terminate its agreement with us if we fail to meet our obligations under these licenses. We may not be able to meet our obligations under these licenses. If we default under any license agreements, we may lose our right to market and sell any products based on the licensed technology.

If we fail to adequately protect our intellectual property, our competitive position could be harmed.

Development and protection of our intellectual property are critical to our business. If we do not adequately protect our intellectual property, competitors may be able to practice our technologies. Our success depends in part on our ability to:

obtain patent protection for our products or processes both in the United States and other countries,

protect trade secrets, and

prevent others from infringing on our proprietary rights.

When polymers are linked, or conjugated, to drugs, the results are referred to as polymer-drug conjugates. We are developing drug delivery technology that links chemotherapy to biodegradable polymers. For example, XYOTAX is paclitaxel, the active ingredient in Taxol®, one of the world s best selling cancer drugs, linked to polyglutamate. We may not receive a patent for all of our polymer-drug conjugates and we may be challenged by the holder of a patent covering the underlying drug and/or methods for its use or manufacture.

The patent position of biopharmaceutical firms generally is highly uncertain and involves complex legal and factual questions. The U.S. Patent and Trademark Office has not established a consistent policy regarding the breadth of claims that it will allow in biotechnology patents. If it allows broad claims, the number and cost of patent interference proceedings in the United States and the risk of infringement litigation may increase. If it allows narrow claims, the risk of infringement may decrease, but the value of our rights under our patents, licenses and patent applications may also decrease. Patent applications in which we have rights may never issue as patents and the claims of any issued patents may not afford meaningful protection for our technologies or products. In addition, patents issued to us or our licensors may be challenged and subsequently narrowed, invalidated or circumvented. Litigation, interference proceedings or other governmental proceedings that we may

become involved in with respect to our proprietary technologies or the proprietary technology of others could result in substantial cost to us. Patent litigation is widespread in the biotechnology industry, and any patent litigation could harm our business. Costly litigation might be necessary to protect a patent position or to determine the scope and

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validity of third-party proprietary rights, and we may not have the required resources to pursue any such litigation or to protect our patent rights. Any adverse outcome in litigation with respect to the infringement or validity of any patents owned by third-parties could subject us to significant liabilities to third-parties, require disputed rights to be licensed from third-parties or require us to cease using a product or technology.

We also rely upon trade secrets, proprietary know-how and continuing technological innovation to remain competitive. Third-parties may independently develop such know-how or otherwise obtain access to our technology. While we require our employees, consultants and corporate partners with access to proprietary information to enter into confidentiality agreements, these agreements may not be honored.

Our products could infringe on the intellectual property rights of others, which may cause us to engage in costly litigation and, if unsuccessful, could cause us to pay substantial damages and prohibit us from selling our products.

We attempt to monitor patent filings but have not conducted an exhaustive search for patents that may be relevant to our products and product candidates in an effort to guide the design and development of our products to avoid infringement. We may not be able to successfully challenge the validity of these patents and could have to pay substantial damages, possibly including treble damages, for past infringement and attorney s fees if it is ultimately determined that our products infringe a third-party s patents. Further, we may be prohibited from selling our products before we obtain a license, which, if available at all, may require us to pay substantial royalties. Moreover, third-parties may challenge the patents that have been issued or licensed to us. Even if infringement claims against us are without merit, or if we challenge the validity of issued patents, lawsuits take significant time, may be expensive and may divert management attention from other business concerns.

We may be unable to obtain the raw materials necessary to produce our XYOTAX product candidate in sufficient quantity to meet demand when and if such product is approved.

We may not be able to continue to purchase the materials necessary to produce XYOTAX, including paclitaxel, in adequate volume and quality. Paclitaxel is derived from certain varieties of yew trees. Supply of paclitaxel is controlled by a limited number of companies. Paclitaxel is available and we purchase it from several sources. We purchase the raw material polyglutamic acid from a single source on a purchase order basis. Should the polyglutamic acid purchased from our sources prove to be insufficient in quantity or quality, should a supplier fail to deliver in a timely fashion or at all, or should these relationships terminate, we may not be able to obtain a sufficient supply from alternate sources on acceptable terms, or at all.

Our dependence on third-party manufacturers means that we do not always have sufficient control over the manufacture of our products.

We do not currently have internal analytical laboratory or manufacturing facilities to allow the testing or production of drug products in compliance with cGMPs. Because we do not directly control our suppliers, these vendors may not be able to provide us with finished product when we need it.

We will be dependent upon these third-parties to supply us in a timely manner with products manufactured in compliance with cGMPs or similar manufacturing standards imposed by foreign regulatory authorities where our products will be tested and/or marketed. While the FDA and other regulatory authorities maintain oversight for cGMP compliance of drug manufacturers, contract manufacturers may at times violate cGMPs. The

FDA and other regulatory authorities may take action against a contract manufacturer who violates cGMPs. One of our products under development,

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XYOTAX, has a complex manufacturing process, which may prevent us from obtaining a sufficient supply of drug product for the clinical trials and commercial activities currently planned or underway on a timely basis, if at all. The active pharmaceutical ingredient and finished product for pixantrone are both manufactured by a single vendor.

If we do not successfully develop additional products, we may be unable to generate significant revenue or become profitable.

We divested our commercial product, TRISENOX, that received marketing approval for relapsed or refractory APL. XYOTAX, pixantrone and CT-2106 are currently in clinical trials and may not be successful. Our STELLAR phase III clinical trials for XYOTAX for the treatment of non-small cell lung cancer failed to meet their primary endpoints. A number of companies in the pharmaceutical industry, including us, have suffered significant setbacks in advanced clinical trials, even after reporting promising results in earlier trials. For example, in our first phase III human trial for lisofylline, completed in March 1998, we failed to meet our two primary endpoints, or goals, even though we met our endpoints in two earlier phase II trials for lisofylline. We will need to commit significant time and resources to develop these and additional product candidates. Our product candidates will be successful only if:

- our product candidates are developed to a stage that will enable us to commercialize them or sell related marketing rights to pharmaceutical companies;
- we are able to commercialize product candidates in clinical development or sell the marketing rights to third parties; and
- our product candidates, if developed, are approved by the regulatory authorities.

We are dependent on the successful completion of these goals in order to generate revenues. The failure to generate such revenues may preclude us from continuing our research and development of these and other product candidates.

If we are unable to enter into new licensing arrangements, our future product portfolio and potential profitability could be harmed.

One component of our business strategy is in-licensing drug compounds developed by other pharmaceutical and biotechnology companies or academic research laboratories. Substantially all of our product candidates in clinical development are in-licensed from a third-party, including XYOTAX, pixantrone and CT-2106.

Competition for new promising compounds and commercial products can be intense. If we are not able to identify future in-licensing opportunities and enter into future licensing arrangements on acceptable terms, our future product portfolio and potential profitability could be harmed.

We may take longer to complete our clinical trials than we expect, or we may not be able to complete them at all.

Before regulatory approval for any potential product can be obtained, we must undertake extensive clinical testing on humans to demonstrate the safety and efficacy of the product. Although for planning purposes we forecast the commencement and completion of clinical trials, the actual timing of these events can vary dramatically due to a number of factors.

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We may not obtain authorization to permit product candidates that are already in the preclinical development phase to enter the human clinical testing phase. Authorized preclinical or clinical testing may not be completed successfully within any specified time period by us, or without significant additional resources or expertise to those originally expected to be necessary. Many drugs in human clinical trials fail to demonstrate the desired safety and efficacy characteristics. Clinical testing may not show potential products to be safe and efficacious and potential products may not be approved for a specific indication. Further, the results from preclinical studies and early clinical trials may not be indicative of the results that will be obtained in later-stage clinical trials. Data obtained from clinical trials are susceptible to varying interpretations. Government regulators and our collaborators may not agree with our interpretation of our clinical trial results. In addition, we or regulatory authorities may suspend clinical trials at any time on the basis that the participants are being exposed to unacceptable health risks or for other reasons. Completion of clinical trials depends on, among other things, the number of patients available for enrollment in a particular trial, which is a function of many factors, including the number of patients with the relevant conditions, the nature of the clinical testing, the proximity of patients to clinical testing centers, the eligibility criteria for tests as well as competition with other clinical testing programs involving the same patient profile but different treatments.

We have limited experience in conducting clinical trials. We expect to continue to rely on third-parties, such as contract research organizations, academic institutions and/or cooperative groups, to conduct, oversee and monitor clinical trials as well as to process the clinical results and manage test requests, which may result in delays or failure to complete trials, if the third-parties fail to perform or to meet the applicable standards.

If we fail to commence or complete, need to perform more or larger clinical trials than planned or experience delays in any of our present or planned clinical trials, including the phase II and phase III clinical trials of pixantrone, our development costs may increase and/or our ability to commercialize our product candidates may be adversely affected. If delays or costs are significant, our financial results and our ability to commercialize our product candidates may be adversely affected.

If we fail to establish and maintain collaborations or if our partners do not perform, we may be unable to develop and commercialize our product candidates.

We have entered into collaborative arrangements with third-parties to develop and/or commercialize product candidates and are currently seeking additional collaborations. For example, we entered into an agreement with the Gynecologic Oncology Group to perform a phase III trial of XYOTAX in patients with ovarian cancer. Additional collaborations might be necessary in order for us to fund our research and development activities and third-party manufacturing arrangements, seek and obtain regulatory approvals and successfully commercialize our existing and future product candidates. If we fail to enter into additional collaborative arrangements or fail to maintain our existing collaborative arrangements, the number of product candidates from which we could receive future revenues would decline.

Our dependence on collaborative arrangements with third-parties will subject us to a number of risks that could harm our ability to develop and commercialize products, including that:

- collaborative arrangements may not be on terms favorable to us;
- disagreements with partners may result in delays in the development and marketing of products, termination of our collaboration agreements or time consuming and expensive legal action;

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- we cannot control the amount and timing of resources partners devote to product candidates or their prioritization of product candidates and partners may not allocate sufficient funds or resources to the development, promotion or marketing of our products, or may not perform their obligations as expected;

- partners may choose to develop, independently or with other companies, alternative products or treatments, including products or treatments which compete with ours;

- agreements with partners may expire or be terminated without renewal, or partners may breach collaboration agreements with us;

- business combinations or significant changes in a partner s business strategy might adversely affect that partner s willingness or ability to complete its obligations to us; and

- the terms and conditions of the relevant agreements may no longer be suitable.

The occurrence of any of these events could adversely affect the development or commercialization of our products.

Because we base several of our drug candidates on unproven novel technologies, we may never develop them into commercial products.

We base several of our product candidates upon novel technologies that we are using to develop drugs for the treatment of cancer. These technologies have not been proven. Furthermore, preclinical results in animal studies may not predict outcomes in human clinical trials. Our product candidates may not be proven safe or effective. If these technologies do not work, our drug candidates may not develop into commercial products.

As a result of our merger with Novuspharma, we are required to comply with the regulatory structure of Italy, which could result in administrative challenges.

As a result of our merger with Novuspharma, our operations need to comply not only with applicable laws of and rules of the United States, including Washington law and the rules and regulations of the SEC and the Nasdaq National Market, but also the European Union legal system and the Republic of Italy, including the rules and regulations of CONSOB and Borsa Italiana, which collectively regulate companies listed on Italy s public markets such as the Nuovo Mercato. Conducting our operations in a manner that complies with all applicable laws and rules will require us to devote additional time and resources to regulatory compliance matters. For example, the process of seeking to understand and comply with the laws of each country, including tax, labor and regulatory laws, might require us to incur the expense of engaging additional outside counsel, accountants and other professional advisors and might result in delayed business initiatives as we seek to ensure that each new initiative will comply with all regulatory regimes.

As a result of our merger with Novuspharma, we are subject to additional legal duties, additional operational challenges and additional political and economic risks related to our operations in Italy.

As a result of our merger with Novuspharma, a portion of our business is based in Italy. We are subject to duties and risks arising from doing business in Italy, such as:

- Italian employment law, including collective bargaining agreements negotiated at the national level and over which we have no control