CELL THERAPEUTICS INC
Form 424B3
April 22, 2004
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Filed pursuant to Rule 424(b)(3)

Registration No. 333-108926

$75,000,000

4% Convertible Senior Subordinated Notes due July 1, 2010

and the common stock issuable upon conversion of the notes

We issued the notes offered by this prospectus in a private placement in June 2003. This prospectus will be used by selling securityholders to resell their notes and the common stock issuable upon conversion of their notes. 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 July 1, 2010. The conversion rate is 74.0741 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 $13.50 per share.

We will pay interest on the notes on January 1 and July 1 of each year. The first interest payment was made on January 1, 2004. The notes are senior in right of payment to our 5.75% Convertible Subordinated Notes due 2008 and rank equally in right of payment with our 5.75% Convertible Senior Subordinated Notes due 2008. The notes are subordinated in right of payment to all of our other existing and future senior debt.

We may provisionally redeem, under the conditions described in this prospectus, some or all of the notes at any time prior to maturity at a redemption price of $1,000 per $1,000 principal amount of notes, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. We will make an additional payment in cash with respect to the notes called for provisional redemption in an amount equal to $280.00 per $1,000 principal amount of notes, less the amount of any interest actually paid on the notes before the date of redemption. In the event of a change in control, as described in this prospectus, you may require us to repurchase any notes held by you.

The notes are not listed on any securities exchange or included in any automated quotation system. The notes are eligible in the PORTAL[SM] Market of the National Association of Securities Dealers, Inc. Our common stock is quoted on the Nasdaq National Market and on the Nuovo Mercato in Italy under the symbol CTIC. On April, 20, 2004, the last reported sale price for our common stock on the Nasdaq National Market was $8.40 per share.

Investing in the notes involves risk. See Risk Factors beginning on page 6.

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 April 21, 2004

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PROSPECTUS SUMMARY

The following is a summary of this prospectus. You should read this entire prospectus carefully, including the documents that we have incorporated by reference, before making an investment decision.

Our Company

We develop, acquire and commercialize novel treatments for cancer. Our goal is to build a leading, vertically integrated biopharmaceutical company with a diversified portfolio of proprietary oncology drugs. Our research, clinical development and in-licensing activities are concentrated on identifying new, less toxic and more effective ways to treat cancer. We currently have one approved cancer drug, TRISENOX, which we market in the U.S. and in the European Union, or EU. TRISENOX has been approved for the treatment of patients with a type of blood cell cancer called Acute Promyelocytic Leukemia, or APL, who have relapsed or failed standard therapies. We have additional clinical trials ongoing related to potential market expansion for this product. We are developing XYOTAX, which utilizes a biodegradable protein polymer to deliver the chemotherapy drug, paclitaxel, more selectively to tumor tissue. We have completed patient enrollment for one pivotal phase III trial and expect to complete enrollment in the first half of 2004 of two more pivotal phase III trials of XYOTAX for the treatment of non-small cell lung cancer. We are also developing Pixantrone, a novel anthracycline with potentially less cardiac toxicity and greater anti-tumor activity than marketed anthracylines. We expect to begin a pivotal phase III trial of Pixantrone for the treatment of aggressive non-Hodgkin s lymphoma in the first quarter of 2004. We are also developing CT-2106 which is entering phase II trials for the treatment of small cell lung cancer and other solid tumors.

On January 1, 2004, we completed our acquisition of Novuspharma, S.p.A., an Italian biopharmaceutical company focused on oncology. Through this acquisition, we obtained worldwide rights to Pixantrone and a high-quality drug discovery organization with an extensive track record in cancer drug development. The Novuspharma acquisition and its drug candidates are consistent with our strategy of growth by strategic acquisition and our goal to develop less toxic more effective cancer therapies.

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, TRISENOX , XYOTAX (formerly referred to as PG-TXL) and Pixantrone 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	$75,000,000 aggregate principal amount of 4% Convertible Senior Subordinated Notes due July 1, 2010 and shares of common stock issuable upon conversion of the notes.
Issuer	Cell Therapeutics, Inc.
Maturity	July 1, 2010
Interest	Interest is payable on the notes at a rate of 4% per year, payable in cash semi-annually on January 1 and July 1 of each year, beginning January 1, 2004.
Conversion	You have the option to convert our notes into shares of our common stock at a conversion rate of 74.0741 shares of common stock per $1,000 principal amount of our notes, which is equivalent to a conversion price of approximately $13.50 per share. The conversion rate is subject to adjustment. 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 redemption or 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 redemption or repurchase, as the case may be. See Description of Notes Conversion Rights.
Ranking	The notes are senior to our existing 5.75% Convertible Subordinated Notes due 2008 and rank equal in right of payment with our existing 5.75% Convertible Senior Subordinated Notes due 2008. The notes are subordinated to our present and future senior debt. As of December 31, 2003, there was outstanding approximately $85.5 million of our 5.75% Convertible Senior Subordinated Notes due 2008 and $29.6 million of our 5.75% Convertible Subordinated Notes due 2008. As of December 31, 2003 our other long-term obligations (excluding deferred revenue) aggregated $5.6 million and our subsidiaries had liabilities (excluding inter-company liabilities) of $2.1 million, of which $0.9 million is included in our $5.6 million of long-term obligations. Our $5.6 million of long-term obligations constitutes all of our senior debt for purposes of the notes as of December 31, 2003. The notes are also effectively subordinated in right of payment to the liabilities of our subsidiaries. The indenture governing the notes does not restrict our incurrence of indebtedness, including senior debt, or our subsidiaries incurrence of indebtedness. See Description of Notes Subordination.

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Provisional Redemption	We may redeem the notes, in whole or in part, at any time prior to maturity at a redemption price equal to $1,000 per $1,000 principal amount of the notes to be redeemed plus accrued and unpaid interest, if any, to, but excluding, the date of redemption if: the closing price of our common stock has exceeded 150% of the conversion price then in effect for at least 20 trading days within a period of 30 consecutive trading days ending on the trading day before the date of mailing of the provisional redemption notice; and the registration statement of which this prospectus forms a part is effective and available for use and is expected to remain effective and available for use for the 30 days following the provisional redemption date, unless registration is no longer required. We will make an additional payment in cash or, at our option, common stock, or in a combination of cash and common stock, with respect to any notes called for provisional redemption in an amount equal to $280.00 per $1,000 principal amount of the notes, less the amount of any interest actually paid on the notes before the date of redemption. We are obligated to make this additional payment on all notes called for provisional redemption, including any notes converted after the notice date and before the provisional redemption date. See Description of Notes Provisional Redemption.
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 in cash or, at our option, in shares of 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 high and low sales prices of the common stock for each of the five trading days ending with the third trading day prior to the repurchase date. A change in control could be an event of default under our senior debt. In those circumstances, the subordination provisions of the indenture under which the notes were issued would likely prevent us from repurchasing the notes until the senior debt is paid in full. 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.

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Events of Default	The following are 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 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 6 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,				
	1999	2000	2001	2002	2003
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, 1999, 2000, 2001, 2002 and 2003, were insufficient to cover fixed charges by $36,280, $51,929, $80,273, $49,903 and $130,031 (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, 2003, we had an accumulated deficit of approximately $433.8 million, not including losses of Novuspharma. We may never become profitable, even if we are able to commercialize additional products. We will need to conduct significant research, development, testing and regulatory compliance activities that, together with projected general and administrative expenses, we expect will result in substantial increasing operating losses for at least the next several years. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

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

We have only one product, TRISENOX, for relapsed or refractory acute promyelocytic leukemia, or APL, that has received marketing approval to date. Our leading drug candidates, TRISENOX for other indications, XYOTAX, Pixantrone and CT-2106, are currently in clinical trials and may not be successful. Even if our drugs progress successfully through initial human testing, they may fail in later stages of development. Many drugs in human clinical trials fail to demonstrate the desired safety and efficacy characteristics. 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. As a result, we are no longer developing lisofylline as a potential product. Many of our drug candidates are still in research and pre-clinical development, which means that they have not yet been tested on humans. 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.

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

We expect that our existing capital resources and the interest earned thereon will enable us to maintain our planned operations through at least early 2005. We expect to receive certain grants and subsidized loans from the Italian government and the European Union through our Italian subsidiary into which Novuspharma s operating assets and liabilities will be contributed. However, we may not receive the relevant funding because the grants and subsidies are awarded at the discretion of the relevant authorities.

Beyond early 2005, or if our plans or assumptions change or are inaccurate, we will have to raise additional funds to continue the development of our technologies and complete the commercialization of products, if any, resulting from our technologies. We may raise such capital through public or private equity financings, partnerships, debt financings, 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 may curtail operations significantly, including the delay, modification or cancellation of research and development programs aimed at bringing new products to market. 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, you may experience dilution of your proportionate ownership of us.

Our operations in Italy make us subject to increased risk regarding currency exchange rate fluctuations.

As a result of our merger with Novuspharma and our consequent operations in Italy, we are exposed to risks associated with foreign currency transactions insofar as we might desire to use U.S. dollars to make contract payments denominated in Euros or vice versa. As the net positions of our foreign currency transactions might fluctuate, our earnings might be negatively affected. In addition, as a result of our merger with Novuspharma, we are exposed to risks associated with the translation of Novuspharma s Euro-denominated financial results and balance sheet into United States dollars. Our reporting currency will remain as the United States dollar, however, a portion of our consolidated financial obligations will arise in Euros. In addition, the carrying value of some of our assets and liabilities will be affected by fluctuations in the value of the United States dollar as compared to the Euro. Changes in the value of the United States dollar as compared to the Euro might have an adverse effect on our reported results of operations and financial condition.

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, both on its own terms, and as compared to the other principal drugs on the market that have the same therapeutic indication. 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.

We may not obtain authorization to permit product candidates that are already in the pre-clinical development phase to enter the human clinical testing phase. Authorized pre-clinical 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 pre-clinical 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 future 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

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to unacceptable health risks. 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 co-operative 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, or experience delays in any of our present or planned clinical trials, including the Phase III clinical trials of XYOTAX, the Phase II clinical trials of TRISENOX and the Phase II and Phase III clinical trials of Pixantrone, our ability to conduct our business as planned could be harmed. Our development costs may increase if we experience any future delays in our clinical trials for XYOTAX, TRISENOX, Pixantrone or our other product candidates or if we need to perform more or larger clinical trials than planned. If delays or costs are significant, our financial results and our ability to commercialize our product candidates may be adversely affected.

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 APL who have relapsed or failed standard therapies, all of our compounds currently are in research or development, and none has been submitted for marketing approval. Our other compounds may not enter human clinical trials on a timely basis, if at all, and we may not develop any product candidates suitable for commercialization.

Prior to commercialization, each product candidate will require significant additional research, development and pre-clinical 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 pre-clinical 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

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. Any 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 we fail to establish and maintain collaborations or if our partners do not perform, we may 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 have entered into an agreement

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with Chugai Pharmaceutical Co., Ltd. to develop and commercialize XYOTAX in several Asian markets. 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;
- 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 many of our product candidates upon novel delivery technologies that we are using to discover and develop drugs for the treatment of cancer. These technologies have not been proven. Furthermore, pre-clinical 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.

We may face difficulties in achieving acceptance of our products in the market if we do not continue to expand our sales and marketing infrastructure.

We currently are marketing TRISENOX with our direct sales force. Competition for these individuals is intense, and in the event we need additional sales personnel, we may not be able to hire individuals with the experience required or number of sales personnel we need. In addition, if we market and sell products other than TRISENOX, we may need to further expand our marketing and sales force with sufficient technical expertise and distribution capacity. If we are unable to expand our direct sales operations and train new sales personnel as rapidly as necessary, we may not be able to increase market awareness and sales of our products, which may prevent us from growing our revenues and achieving and maintaining profitability.

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If any of our license agreements for intellectual property underlying TRISENOX, 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 Memorial Sloan-Kettering Cancer Center, Samuel Waxman Cancer Research Foundation, Beijing Medical University, The University of Vermont, Hoffman La Roche and others, including the intellectual property relating to TRISENOX and 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 protect adequately 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 drugs 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 our polymer-drug conjugates and we may be challenged by the holder of a patent covering the underlying drug.

The patent position of biopharmaceutical firms generally is highly uncertain and involves complex legal and factual questions. The United States 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 our orphan drug designations in the United States or EU, which are designations for products meeting criteria based on the size of the potential United States or EU patient population for a drug, respectively, and which entitle that drug to seven years of exclusive rights in the United States market or ten years in the EU market, as applicable, or to protect a patent position or to determine the scope and 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.

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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 we are not successful, could cause us to pay substantial damages and prohibit us from selling our products.

We attempt to monitor the patent filings 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 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.

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 TRISENOX, XYOTAX and Pixantrone. 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 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. We purchase the majority of the paclitaxel we need from a single vendor. We also purchase the raw material polyglutamic acid from a single source on a purchase order basis. Should the paclitaxel or polyglutamic acid purchased from our sources prove to be insufficient in quantity or quality, 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 may not have sufficient control over the manufacture of our products.

We do not currently have internal facilities for the GMP manufacture of any of our development or commercial products. In addition, TRISENOX, our first commercial product, is currently manufactured by a single vendor. In 2002, we began the process of qualifying an additional supplier for our finished product manufacturing for TRISENOX. This additional supplier received FDA approval to manufacture TRISENOX in June 2003. Because we do not directly control our suppliers, these vendors may not be able to provide us with finished product when we need it. Plans are in place to develop additional manufacturing resources, such as entering into collaborative arrangements with other parties that have established manufacturing capabilities or elect to have other additional third parties manufacture our products on a contract

basis.

We will be dependent upon these third parties to supply us in a timely manner with products manufactured in compliance with current good manufacturing practices, or cGMPs, or similar manufacturing standards

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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. Such actions may include requiring the contract manufacturer to cease its manufacturing activities.

Another one of our products under development, 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.

We are subject to extensive government regulation, including the requirement of approval before our products may be marketed.

Regulatory agencies have approved only one of our products, TRISENOX, for sale in the United States and the European Union, to treat patients with a type of blood cancer called acute promyelocytic leukemia, or APL, who have relapsed or failed standard therapies. Before we can market TRISENOX for other indications in the United States, or EU, we must obtain additional FDA approval and/or approval of the European Agency for the Evaluation of Medical Products, or the EMEA. Our other products are in development, and will have to be approved by the FDA before they can be marketed in the United States and by the EMEA before they can be marketed in the EU. Obtaining FDA or other national regulatory approval requires substantial time, effort and financial resources, and we may not obtain approval on a timely basis, if at all. If the FDA or the EMEA do not approve our developmental products and any additional indications for marketed products in a timely fashion, or does not approve them at all, our business and financial condition may be adversely affected.

In addition, we and our currently marketed products and product candidates are subject to comprehensive regulation by the FDA and the EMEA. Regulation by the FDA and EMEA begins before approval for marketing is granted and continues during the life of each product. For example, TRISENOX was approved by the FDA under its accelerated approval process and by the EMEA under exceptional circumstances and we committed to completing several post-approval requirements to both the FDA and the EMEA, including the conduct of additional clinical studies. If we fail to fulfill these obligations, the FDA or EMEA may withdraw approval of TRISENOX. In addition, the FDA and other regulatory authorities regulate, for example, research and development, including pre-clinical and clinical testing, safety, effectiveness, manufacturing, labeling, advertising, promotion, export, and marketing of our products. Manufacturing processes must conform to 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. Also, a drug may not be promoted for other than its approved indication, and the FDA, EMEA and other regulatory authorities may institute enforcement actions against companies that do so. Our failure to comply with this or other FDA or other regulatory requirements may result in various adverse consequences, including possible delay in approval or refusal to approve a product, recalls, seizures, withdrawal of an approved product from the market, and/or the imposition of civil or criminal sanctions.

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 its employees from participation in federal and state health care programs. Although we have policies prohibiting violations of relevant regulations and statutes, unauthorized actions of our employees or consultants, or unfavorable interpretations of such regulations or statutes may result in third parties or regulatory agencies bringing legal proceedings or enforcement actions against us.

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 now 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 Securities and Exchange Commission and the Nasdaq National Market, but also the EU legal system and the Republic of

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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 both regulatory regimes.

As a result of our merger with Novuspharma, we are subject to new legal duties 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;
- EU data protection regulations, under which we will be unable to send private personal data, including many employment records and some clinical trial data, from our Italian offices to our United States offices until our United States offices self-certify their adherence to the safe harbor framework established by the United States Department of Commerce in consultation with the European Commission;
- tariffs, customs, duties and other trade barriers; and
- capital controls, terrorism and other political risks.

These risks related to doing business in Italy could harm the results of our operations.

Uncertainty regarding third party reimbursement and health care cost containment initiatives may limit our returns.

The ongoing efforts of governmental and third party payors to contain or reduce the cost of health care may affect our ability to commercialize our products successfully. Governmental and other third party payors are increasingly attempting to contain health care 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;

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 health care 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

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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. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the adoption of such proposals could make it difficult or impossible to sell our products. TRISENOX has been reimbursed by third party payors, but there is no guarantee this reimbursement will continue.

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 markets. 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, which are drugs that inhibit cell growth by stopping cell division and are widely used as treatments for cancer. Many oncology-focused multinational corporations currently market or are developing taxanes, epothilones, which inhibit cancer cells by a mechanism similar to taxanes, or similar products (including, among others, Bristol-Myers Squibb Co., which markets Taxol®, one of the best-selling cancer drugs and Aventis, which markets Taxotere®. In addition, several companies are also developing novel taxanes and formulations which could compete with our products.

In the hematology market, we hope to receive approval to market TRISENOX to larger indications than currently authorized. We will face competition from a number of biopharmaceutical companies, including:

Celgene Corporation, which currently sells thalidomide used in the treatment of multiple myeloma, a cancer of the bone marrow, and is developing ImiDs;

Millennium Pharmaceuticals, Inc., which recently launched Velcade for treatment of multiple myeloma;

Pharmion Corporation, which has signed an agreement with Celgene to expand internationally the marketing of thalidomide and is developing 5-Azacytidine for myelodyplastic syndromes, or MDS, also known as smoldering leukemia or preleukemia, which are a group of diseases in which the bone marrow does not function normally, and insufficient numbers of mature blood cells are in circulation; and

SuperGen Corporation, which is developing decitabine, which is in phase III studies in MDS.

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 chemotherapy drugs. 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, including Vincristine Sulfate Liposome for Injection, or VSLI, a product being developed by Inex Pharmaceuticals Corporation that is currently in late stage clinical trials.

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, to be less expensive, to have fewer side

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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.

If we lose our key personnel or we are unable to attract and retain additional personnel, we may be unable to pursue collaborations or develop our own products.

We are highly dependent on Dr. James A. Bianco, our president and chief executive officer, Dr. Jack W. Singer, our chief medical officer and Silvano Spinelli, our executive vice president of development and managing director of european operations. The loss of any one of these principal members of our scientific or management staff, or failure to attract or retain other key scientific employees, could prevent us from pursuing collaborations or developing and commercializing our products and core technologies. Recruiting and retaining qualified scientific personnel to perform research and development work are critical to our success. There is intense competition for qualified scientists and managerial personnel from numerous pharmaceutical and biotechnology companies, as well as from academic and government organizations, research institutions and other entities. In addition, we will rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development strategy. All of our consultants and advisors will be employed by other employers or are self-employed, and will have commitments to or consulting or advisory contracts with other entities that may limit their availability to us.

The integration of Novuspharma s business and operations will be a challenging, complex, time-consuming and expensive process and may disrupt our business if not completed in a timely and efficient manner.

The challenges involved in the integration of Novuspharma include the following:

- effectively pursuing the clinical development and regulatory approvals of all product candidates while effectively marketing our current approved product (TRISENOX);
- successfully commercializing products under development and increasing revenues from TRISENOX;
- retaining certain existing strategic partners;
- retaining and integrating management and other key employees;
- coordinating research and development activities to enhance introduction of new products and technologies;
- integrating purchasing and procurement operations in multiple locations;
- maintaining an adequate level of liquidity to fund our continuing operations and expansion;
- integrating the business culture of Novuspharma with our culture and maintaining employee morale;

transitioning all facilities to a common information technology system;

developing and maintaining uniform standards, controls, procedures and policies relating to financial reporting and employment related matters that comply with both United States and Italian laws and regulations;

maintaining adequate focus on the core business of the combined company while integrating operations;

maintaining relationships with employees, strategic partners, manufacturers and suppliers while integrating management and other key personnel;

realizing the benefits and synergies to the extent or in the time frame anticipated; and

coping with unanticipated expenses related to integration.

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We may not succeed in addressing these challenges or any other problems encountered in connection with integration following the merger, which may be exacerbated by the geographic separation of our operations in the United States and in Italy. If management is not able to address these challenges, we may not achieve the anticipated benefits of the merger, which may have a material adverse effect on our business and could result in the loss of key personnel.

Our limited operating experience may cause us difficulty in managing our growth and could seriously harm our business.

As a result of additional trials for TRISENOX for indications other than relapsed or refractory APL and clinical trials currently underway for XYOTAX, Pixantrone and our other products in development, we have expanded our operations in various areas, including our management, regulatory, clinical, financial and information systems and other elements of our business process infrastructure. We may need to add additional key personnel in these areas. In addition, as growth occurs, it may strain our operational, managerial and financial resources. We may not be able to increase revenues or control costs unless we continue to improve our operational, financial, regulatory and managerial systems and processes, and expand, train and manage our work force.

Because there is a risk of product liability associated with our products, we face potential difficulties in obtaining insurance.

Our business exposes us to potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceutical products, and we may not be able to avoid significant product liability exposure. While we have insurance covering product use in our clinical trials, and currently have product liability insurance for TRISENOX, it is possible that we will not be able to maintain such insurance on acceptable terms or that any insurance obtained will provide adequate coverage against potential liabilities. Our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or limit the commercialization of any products we develop. A successful product liability claim in excess of our insurance coverage could exceed our net worth.

Since we use hazardous materials in our business, we may be subject to claims relating to improper handling, storage or disposal of these materials.

Our research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be eliminated completely. In the event of such an accident, we could be held liable for any damages that result and any such liability not covered by insurance could exceed our resources. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development or production efforts.

We may not be able to conduct animal testing in the future, which could harm our research and development activities.

Certain of our research and development activities involve animal testing. Such activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting activities through protests and other means. To the extent the activities of these groups

are successful, our business could be materially harmed by delaying or interrupting our research and development activities.

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Risks Related to the Securities Markets

Our stock price is extremely volatile, which may affect our ability to raise capital in the future.

The market price for securities of biopharmaceutical and biotechnology companies, including ours, historically has been highly volatile, and the market from time to time has experienced significant price and volume fluctuations that are unrelated to the operating performance of such companies. For example, during the twelve months ended December 31, 2003, our stock price ranged from a low of $5.18 to a high of $15.70. Fluctuations in the trading price or liquidity of our common stock may adversely affect our ability to raise capital through future equity financings.

Factors that may have a significant impact on the market price and marketability of our common stock include:

- announcements of technological innovations or new commercial therapeutic products by us, our collaborative partners or our present or potential competitors;
- our quarterly operating results;
- announcements by us or others of results of pre-clinical testing and clinical trials;
- developments or disputes concerning patent or other proprietary rights;