

CELL THERAPEUTICS INC  
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The following press release was issued by Cell Therapeutics, Inc. ( CTI ) on November 19, 2003. The referenced Novuspharma S.p.A. press release is filed herewith and immediately follows the CTI press release.

**Pixantrone Research Study Reveals No Increase in**

**Anthracycline-Induced Heart Damage**

**Nov. 19, 2003 Seattle** Novuspharma S.p.A. (Novuspharma) (Nuovo Mercato: NOV.MI) announced the results of a preliminary preclinical study on Pixantrone together with results from three other studies of Pixantrone, which were presented in a poster session at the AACR-NCI-EORTC, International Conference on Molecular Targets and Cancer Therapeutics in Boston, Massachusetts, on Tuesday, November 18. In June, Cell Therapeutics, Inc. (CTI) (Nasdaq: CTIC) and Novuspharma announced they had entered into a merger agreement.

For more information on the study, refer to the Novuspharma website at:

<http://www.novuspharma.com/nov/investorinfo/releases/>

**About Cell Therapeutics, Inc.**

Based in Seattle, CTI is a biopharmaceutical company committed to developing an integrated portfolio of oncology products aimed at making cancer more treatable. For additional information, please visit [www.cticseattle.com](http://www.cticseattle.com).

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**Study reveals no increase in anthracycline-induced heart damage with Pixantrone**

*Preclinical study supports preliminary clinical data suggesting Pixantrone is safe in anthracycline pre-treated patients*

**Milan, Italy, 19 November 2003** Novuspharma SpA (Nuovo Mercato: NOV.MI and NOV.IM), a biopharmaceutical company focused on developing new cancer therapeutics, today announces preclinical results which demonstrate that Pixantrone does not significantly increase existing anthracycline-induced heart damage, while repeat treatment with traditional anthracyclines leads to significant deterioration in heart tissue. These results suggest Pixantrone is safe to use in patients heavily pre-treated with existing anthracyclines; the same conclusion that has been reached in clinical trials for Pixantrone in relapsed aggressive non-Hodgkin's lymphoma (NHL). The results together with results from three other studies with Pixantrone, were presented in a poster session at the AACR-NCI-EORTC, International Conference on Molecular Targets and Cancer Therapeutics in Boston, Massachusetts, on Tuesday November 18, from 12:30 to 19:30 local time.

Pixantrone is an investigational drug that is being developed by Novuspharma to improve the activity and safety of anthracyclines. Anthracyclines form an important treatment for a number of malignancies but their utility is often limited by their potential to cause irreversible heart damage, which often prevents them being used in repeat therapy. Pixantrone was specifically designed to eliminate the cardiac toxicity associated with these agents. It is currently undergoing a number of clinical trials in NHL with the aim of providing a highly active anthracycline-like agent, which could be safely used in patients previously treated with traditional anthracyclines (such as mitoxantrone and doxorubicin).

**Pixantrone does not increase existing anthracycline-induced heart damage in preclinical models**

Results were presented in Boston from a preclinical model designed to mimic the administration of Pixantrone to relapsed patients, which have previously been treated with the traditional anthracyclines. In this experiment, doxorubicin pre-treated mice were administered Pixantrone, doxorubicin, mitoxantrone or vehicle (inactive injection), following a six-week treatment-free period. Damage to the heart tissue was scored using the Bertazzoli method, which runs from 0 (normal) to 10 (severe damage). The results demonstrate that animals which received a second cycle of treatment with Pixantrone had a mean cardiotoxicity score that was not significantly different from animals receiving vehicle alone (2.6 with Pixantrone in the second cycle, compared to 2.7 with vehicle ( $p=0.91$ )). In contrast, a second cycle of treatment with mitoxantrone or doxorubicin led to a statistically significant difference in cardiac damage compared to vehicle treated animals (mean score of 5.7, with doxorubicin ( $p=0.0029$ ) and 8.4 with mitoxantrone ( $P<0.0001$ )). Results were also statistically significant when animals receiving Pixantrone in their second cycle were compared to those receiving doxorubicin ( $p=0.0011$ ) and mitoxantrone ( $p<0.0001$ )\*.

These results therefore suggest it would be safe to use Pixantrone in patients which have been heavily pre-treated with the traditional anthracyclines; a similar conclusion has been drawn from the clinical studies conducted for Pixantrone in relapsed patients to date.

**In contrast to Pixantrone, doxorubicin appears to induce the expression of p21 in heart tissue; a response associated with cellular stress**

Novuspharma has conducted a large number of experiments confirming that Pixantrone causes no meaningful heart damage in anthracycline naïve animals, while the traditional anthracyclines are markedly cardiotoxic. At the congress, results were

presented from an experiment where the gene expression profile of mouse heart tissue was monitored during treatment with Pixantrone or doxorubicin. As expected, doxorubicin treatment led to significant cardiac damage, while no injury was detected in Pixantrone treated animals. The experiment also revealed that doxorubicin modified the expression of several genes, including the induction of p21, which is indicative of cellular stress. Pixantrone did not induce the expression of p21 and only slightly affected gene expression, with results similar to those observed with vehicle alone.

In total, 4 presentations were made at AACR-NCI-EORTC on November 18, from 12:30 to 19:30 local time:

The aza-anthracenedione Pixantrone (BBR 2778) confirms its reduced cardiotoxic potential vs. reference standards also in mouse pre-treated with anthracyclines. L. Crippa et al.

Molecular and histopathological evaluation of lack of Pixantrone induced cardiotoxicity as compared to Doxorubicin in mice. M. Cassin et al.

Investigation of Pixantrone's mechanism of action on HS-Sultan human non-Hodgkin's lymphoma cells by cDNA microarray technology. M. Cassin et al.

Population pharmacokinetics of Pixantrone in cancer patients. A. Bernareggi et al.

\*These results were achieved using a daily doxorubicin dose of 4.6 mg/kg in both cycles but similar conclusions can be drawn from animals treated at 7.5mg/kg of doxorubicin.

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#### **Notes to Editors**

#### **Novuspharma SpA and its merger agreement with Cell Therapeutics (CTI)**

Novuspharma, based in Bresso, Milan, is an emerging biopharmaceutical company leveraging its expertise in the field of oncology to discover and develop innovative new treatments for cancer. It has three products in clinical development and a dynamic research programme. Novuspharma was established in 1998 following the merger of Boehringer Mannheim and Hoffmann-La Roche, to exploit the R&D team's

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proven track record in product development. On June 17<sup>th</sup>, 2003, Novuspharma announced it had signed a merger agreement with Cell Therapeutics (CTI) (NASDAQ CTIC) of Seattle. CTI is a public biopharmaceutical company, which markets TRISENOX<sup>®</sup> in the US and Europe and is developing XYOTAX (CT-2103), which is in pivotal phase III trials for lung cancer. For further information, please visit the Company's website at [www.novuspharma.com](http://www.novuspharma.com).

For an explanation of technical terms please see [www.novuspharma.com/nov/glossary/](http://www.novuspharma.com/nov/glossary/)

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CAUTIONARY STATEMENT REGARDING FORWARD LOOKING STATEMENTS

This press release contains forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are based on management's current expectations and beliefs and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. The forward-looking statements contained in this press release include statements about future financial and operating results, the proposed CTI/Novuspharma merger, and risks and uncertainties that could affect CTI's product and products under development. These statements are not guarantees of future performance, involve certain risks, uncertainties and assumptions that are difficult to predict, and are based upon assumptions as to future events that may not prove accurate. Therefore, actual outcomes and results may differ materially from what is expressed herein. For example, if either of the companies fail to satisfy conditions to closing, the transaction will not be consummated. In any forward-looking statement in which CTI expresses an expectation or belief as to future results, such expectation or belief is expressed in good faith and believed to have a reasonable basis, but there can be no assurance that the statement or expectation or belief will result or be achieved or accomplished. The following factors, among others, could cause actual results to differ materially from those described in the forward-looking statements: risks associated with preclinical, clinical and sales and marketing developments in the biopharmaceutical industry in general and in particular including, without limitation, the potential failure to meet TRISENOX® revenue goals, the potential failure of XYOTAX to prove safe and effective for treatment of non-small cell lung and ovarian cancers, the potential failure of TRISENOX® to continue to be safe and effective for cancer patients, determinations by regulatory, patent and administrative governmental authorities, competitive factors, technological developments, costs of developing, producing and selling TRISENOX® and CTI's products under development in addition to the risk that the CTI and Novuspharma businesses will not be integrated successfully; costs related to the proposed merger; and other economic, business, competitive, and/or regulatory factors affecting CTI's and Novuspharma's businesses generally, including those set forth in CTI's filings with the SEC, including its Annual Report on Form 10-K for its most recent fiscal year and its most recent Quarterly Report on Form 10-Q, especially in the Factors Affecting Our Operating Results and Management's Discussion and Analysis of Financial Condition and Results of Operations sections, its Current Reports on Form 8-K and its filings on Forms S-3 and S-4. CTI is under no obligation to (and expressly disclaims any such obligation to) update or alter its forward-looking statements whether as a result of new information, future events, or otherwise.