

Edgar Filing: CELL THERAPEUTICS INC - Form 425

CELL THERAPEUTICS INC  
Form 425  
November 13, 2003

Filed by Cell Therapeutics, Inc.

Pursuant to Rule 425 under the Securities Act of 1933

Subject Company: Cell Therapeutics, Inc.

Commission File No.: 001-12465

The following is a transcript of a presentation that was given by Cell Therapeutics, Inc. at the CIBC World Markets Fourteenth Annual Healthcare Conference on November 11, 2003.

Matt Geller: Good morning. I'm Matt Geller, Senior Biotech Analyst from CIBC World Markets. As required, since I'm going to do a formal introduction, I have to do disclosures, first of all. So, CIBC World Markets does not own more than 1% of Cell Therapeutics. We have done investment banking for them. I don't own any stock, but my 5-year-old actually does own stock, and he's a fantastic stock picker. So, anyway that's true.

Anyway, I'd like to introduce Jim Bianco, the President and CEO of Cell Therapeutics. This is a company that has tremendous diversity in the cancer area, which I think is far from recognized at this point. We are heading towards a very important year for Cell Therapeutics, a really critical year with the XYOTAX data coming out. And if this data does look anything like the phase II data that we've seen thus far, this is going to be an extremely important huge product for Cell Therapeutics; that, on top of TRISENOX<sup>®</sup>, which is meeting and beating expectations now. And I think the other really important hidden asset here is Novuspharma, I think. Since it's an Italian company I think people here don't necessarily know that I was in Italy recently. It's very well-known and very well-respected, some really strong people, and a product in phase III, Pixantrone, with phase III data coming in 2005 also with enormous potential. So, within a couple of years, this is a company that has the potential of three products on the market and some really blockbuster sales.

It's a pleasure to introduce Jim Bianco, who has done a great job of putting together a really major cancer company.

Mr. Bianco: Thank you, Matt. Good morning. As usual, before I get started, let me remind you that I will be making forward-looking statements, and as such, I refer you to our SEC filings for more information about the company and its programs. I'd also like to remind you that we do have an active registration statement with the SEC pertaining to our recently-approved merger with Novuspharma.

As you heard, we do have an approved product called TRISENOX<sup>®</sup>. That product continues to do very well. We've put up the guidance for \$24 million in net revenues this year. We're pretty confident that we can make that number. We also have the potential as you'll see to look for label expansion outside of its initial indication, and I'll review with you some of the data that will be coming up at ASH: why we believe this product can get regulatory

approval and other indications, such as MDS and in certain subsets of patients with multiple myeloma.

As Matt noted, clearly all eyes are on XYOTAX. We have three large phase III studies, one which is nearing completion in lung cancer, and I'll update you on some of that data as well. And as you know, this was the first product that the prestigious Gyn Oncology Group had selected to put into a phase III study through their cooperative network, and we should have some news updating you on their status with the FDA on that phase III trial as well.

And then, lastly, the newest addition to our product pipeline is from our Novuspharma merger, which is called Pixantrone, and actually we have some very exciting data that we'll preview what's coming up at ASH as well.

2106, we shouldn't forget that the second polyglutamate candidate that we have put into the clinic is our polyglutamate camptothecin. The data from the phase I studies will actually be previewed next week at the EORTC, and our phase II program will be outlined at that time. We ended the quarter in a strong financial position, as you can see, on a pro forma basis about \$225 million in cash.

As Matt said, we have multiple shots on goal, not just with an approved product. We are trying to expand market share, but with two very attractive late-stage product candidates that we think could be commercially very exciting for this company.

Let's talk a little bit about TRISENOX. As you may know, this is the product that we market here in the U.S. We don't really promote it very aggressively in Europe, although now with the Novuspharma merger we certainly have a physical presence to go after that market a little bit more aggressively next year. It is a profitable operating business, and it costs us about \$19 or 20 million to run that business completely in the U.S. and in Europe, and some \$24 million in net sales that will meet our goal this year of making it a profitable business. We continue to invest in this product. We continue to see combination therapy demonstrate that this product may, in fact, be a very useful therapeutic in such diseases not only like APL, but also in the MDS studying myeloma, and then as you saw from Stanford University's recent release some very provocative data in combination with radiation in glioblastoma.

This chart just shows our 2001 and '02 performance. The estimate for '03 is, as we have cited, \$24 million in net sales. And then, as you can see, the range for next year, we have not provided guidance. We typically will do that on our fourth quarter conference call, but they range from a low of \$27 million to a high of \$43 million for net sales, and we're pretty confident that we will

continue to see at least the type of multiple growth that we have experienced of late.

If you look at the uses patterns for this product, as you can see year-to-date, the same period last year versus 03, we were watching the MDS application for usage patterns really become the predominant sales pattern for this product right now. Multiple myeloma, as we mentioned on the conference call, was a little soft following the Velcade launch, and that was for the most part made up by an increase in the MDS application. APL is obviously pretty flat, and we think we own the relapsed APL market. And we have some plans on expanding this into the front-line APL market, as you'll see from data from M.D. Anderson, that factor in combination with TRISENOX, thereby the leading chemotherapy in the front-line treatment setting at a 80% complete remission rate, which was molecular remissions durable at one year; thus, suggesting that you may not have to expose patients to chemotherapy in the front-line treatment of APL. And we are further exploring the implications of that ASH abstract, if you will, of that study with our medical affairs group, and ultimately with the regulatory bodies.

This just gives a snapshot of some of the data that was presented in MDS. Again, we have two large studies that are completing. They are randomized trials in the U.S. and in Europe. We're seeing about a 28% to 30% response rate, importantly not just in the so-called low-risk category, which is the relatively smaller incidence of MDS, but even amongst the high-risk patients, the so-called high IPSS scores. Importantly, those patients that do respond have very durable transfusion independence, sometimes lasting more than two years, on average about a year. And then, as I mentioned, we have been exploring with the FDA requirements for either one or two of these studies potentially being useful for a label expansion in an MDS indication.

This is pilot study data that Jim Berenson has put into an ASH abstract, and this is why we think that this product can become a significant player in the multiple myeloma space, which right now is a relatively third-line or salvage setting. This is where the product is being utilized, but clearly, as we show here, this is a study with patients who have melphalan, Thalidomide and Velcade failures. He showed that all ten of these patients, when given TRISENOX® and low-dose melphalan in combination with vitamin C, had a significant decrease in their so-called myeloma protein. These would all be PRs or significant PRs using the current classification schema. Five patients who had significant renal dysfunction all had significant improvement, up to 65% improvement in their kidney failure. And most importantly, if you look at the durability, six of the ten patients have durable ongoing responses, some out past a year. So, although it's a relatively small sample, clearly a very strong signal in a very low dose of melphalan in patients who have resistant disease. And if you recall the Velcade study, the summit trial was one in which they gave Velcade. If you failed Velcade after two cycles, you went on

to get steroids. That single non-randomized trial was ultimately the summary basis for their approval, but we obviously will explore with the agency as we expand this study into a multi-center trial the implications of those findings.

Now we move on to talk about Pixantrone. Just to remind you, Pixantrone belongs to a class of agents called DNA intercalators. Anthracyclines are the third or fourth most frequently used class of anti-cancer agents, and they are actually curative in the settings of treating leukemia, lymphomas, and in certain stages of breast cancer. They do about \$500 million in annual sales worldwide, despite the fact that it is a multi-source product market. And the most important limitation for anthracyclines as a class is that if you're not cured on the first exposure—meaning the first regimens that you typically chop or the so-called anthracycline (inaudible) for breast cancer, that you cannot receive any more anthracycline because there is a lifetime cap on the total exposure because of the severity of irreversible heart damage that can occur if you get re-exposed to anthracyclines in this class of agents. So, clearly, an agent that has less cardiac toxicity has the potential not only of being used in a relapse setting, but actually replacing front-line anthracyclines in diseases like lymphoma, breast cancer, and leukemia.

The bottom part of this slide just shows the effect of Herceptin, as you know, agents that also cause cardiac toxicity, and it cannot be used in combination with anthracyclines because they increase the incidence of cardiac side effects. And that is why Herceptin has predominantly been used either as a single agent or used in the salvage setting with paclitaxel, and is not used in the front-line setting of metastatic breast cancer, the much bigger market potential for that product, because of the combined toxicities when you give Herceptin and anthracyclines in that population in terms of cardiac toxicity.

So, what Novuspharma did, quite creatively, was look at the part of the anthracycline class and molecule that's responsible for its anti-tumor activity, and then to dissect out those domains that they believed were responsible for the cardiac toxicity. And in doing so, they developed Pixantrone, which had in preclinical models no propensity compared to control animals for inducing cardiac damage. And importantly, in animals that had cardiac damage induced with anthracycline, there was a very small increase of re-exposure with Pixantrone to those animals in terms of cardiac toxicity as compared to a very significant increase on re-exposure for so-called doxorubicin prior treated animals.

If you look at the treatment algorithms for non-Hodgkin's lymphoma in particular, you can see that aggressive non-Hodgkin's lymphoma makes up the majority of this market. I'm sure you're all familiar with the indolent lymphoma and Rituxan that is predominantly the mainstay therapy in the indolent disease. In aggressive, however, since it is a curable disease, CHOP is pretty much the cornerstone therapy and front line. There are certainly some

data I think somewhat disappointing about our CHOP that was reported, the ECOG study the abstract that came out at ASH this year. But importantly, about 30% to 40% of patients will get cured with CHOP in the front-line treatment setting. The majority, however, do relapse, and once they relapse they cannot be reintroduced to an anthracycline, so they typically get other regimens that don't contain anthracycline. And ultimately in the third-line or salvage setting, there are no approved agents for treating relapsed aggressive lymphoma.

So, Novuspharma has been predominantly going essentially after that treatment algorithm. Initially, the panel on the left demonstrating that in multiple relapse, resistant, or refractory aggressive non-Hodgkin's lymphoma, a single agent, Pixantrone, actually induced a very high rate of objective responses with 20% complete remission and 16% partial remission. This is clearly the best single agent activity that's been reported in the literature. Most importantly, those remissions are durable. They lasted on average about 11 months, meaning that time to progression was 11.8 months in that trial.

In addition, they reported at the ISEH meetings earlier this year that if you took patients who failed front-line and second-line therapies, and now instituted took the standard so-called ESHAP or DSHAP regimen, but substituted Pixantrone for the etoposide that they can induce, again, a very high rate of objective responses, about 66% of those patients, with a third of them being complete remissions. And that study is obviously in a phase II trial right now, trying to demonstrate the fact that the complete remission rate in a third-line treatment setting, salvage, in a multi-agent trial could be beneficial to patients with lymphoma.

This is a preview of data that will be presented at ASH. You saw a press release from Novuspharma yesterday about the abstract information. This is an update as of September. This is a phase I study. They took patients who failed CHOP. All of them were not eligible to receive anthracyclines; again, because they had pretty much reached the 450 to 500 mg/m<sup>2</sup> maximum exposure level. And then, in a dose-dependent phase I fashion they were able to demonstrate a very high rate of response. In fact, the objective response rate in this, albeit small, cohort of 22 patients was 79%, but the impressive aspect of this is that 53% of them were complete remissions. This study is now enrolling into a phase II component. Clearly, in the relapse CHOP setting, these are second to seventh-line relapses. They did not see cardiac toxicity in this population. I think this data is very encouraging that Pixantrone may, in fact, be a safer, more active anthracenedione of the class of DNA intercalators.

The registration strategy for us is pretty straightforward. We've had our meeting with the FDA. We have a very clear guideline of what they would like to see, what the thought leaders are encouraging us to do with this stage,

and given this activity and the durability of that activity. We believe that a third-line salvage pivotal trial can be our quickest route to market with this product. We have been told that it would qualify for accelerated approval under a so-called sub-part H, and we are now in the final process of submitting our SPA package to the FDA, which we plan on doing after our investigators meeting at ASH in early December. As you can see, we also have studies that are ongoing in second line, and then a proposed study now that we have data in the failed or relapsed CHOP failures of activity, but there has been a lot of interest and encouragement to put this into front line, replacing doxorubicin in the front-line treatment setting for aggressive lymphoma.

And then lastly, there are some studies that are planned with the folks at Hopkins to look at a phase I study in metastatic breast, and this time now allowing Herceptin to be used in combination with an anthracycline.

And this just shows the break up. If you look and, again, remember this is generic price on the doxorubicin, which pretty much owns the lymphoma and the leukemia space Epirubicin is the predominant or elements of the predominant anthracycline in breast cancer.

I'm going to close by updating you on our XYOTAX This is our polyglutamate paclitaxel program. Genentech is doing a great job of educating the clinical community about the differences in blood vessels between blood vessels in tumors versus normal tissue. Again, pictorially on the right, a tumor vasculature typically has holes. They're porous. The whole science here behind the polyglutamate technology is that you have a molecule that's big enough like a polymer. As it's injected, it circulates in the blood stream, and it will get preferentially distributed to and trapped in tumor tissue because of the differences in their blood vessels.

So, if you now link chemotherapy to that polymer, you have a way to do two things. One, get more of the chemotherapy preferentially to the target tissue, which is the tumor. And because the chemotherapy is covalently linked to the polymer, the blood levels of free chemotherapy should be much lower than a standard formulation of a product or the marketed product. And that should translate into a lower side effect profile, specifically those side effects that are responsible from a so-called maximum concentration of exposure, such as hair loss, neutropenia, and the so-called hypersensitivity reactions.

What we and others have also shown and this is actually some interesting metabolic data that will be presented next week at the EORTC meeting is that the polymer, unlike the formulation, doesn't diffuse into the tumor cell, but is actively taken up through a process called pinocytosis. And then once inside the so-called liposomal vesicles, enzymes that are rich in these metabolically-active tissues, like tumor tissue, will actually digest the polymer

backbone and releasing the paclitaxel predominantly inter-cellularly. And from a mechanistic standpoint, this has a lot of potential to provide not just the profile that is potentially safer in terms of acute side effects, but will allow obviously the drug to work in settings where standard formulations of paclitaxel may not work.

And this is the target product profile that we have continued to see now in over 350 patients in our phase I and II studies. As you know, we don't require pre-medications for the most part. Hypersensitivity reactions have been far and few. I think there have been literally 3 reported out of the 350 patients, and remember, they're not getting routinely pre-medicated, and when they do experience a hypersensitivity reaction, it's mild, never typically the grade III variety. Infusion time, 10 minutes, peripheral vein. It doesn't require, again, a large catheter. We do not see hair loss with single-agent drugs, including at doses as high as 250 to 270 mg/m<sup>2</sup>.

We have, as I'll show you later, a much lower incidence of severe neutropenia than standard paclitaxel. Neuropathy, since this is typically a side effect that is more total dose exposure related than it is to the so-called maximum or the dose intensity that you're giving, we see it, but we see it significantly less frequently than what you would at equivalent exposures to paclitaxel. And as a result of that profile, this product is much more tolerable than standard formulated paclitaxel, both alone and in combination.

As you know, the first disease enemy that we're pursuing is lung cancer. The rationale for that is pretty straightforward. Paclitaxel, not docetaxel, but paclitaxel is pretty much the cornerstone for front-line treatments of lung cancer, including both the high-risk and the low-risk patients. We'll talk a little bit about the so-called high-risk in a second. In the second-line treatment setting, most patients have failed front-line paclitaxel platinum-containing regimens. Taxotere is the only approved agent. However, because of the milder side effect profile, Gemcitabine does share a piece of that market, certainly in the United States and certainly predominantly in Europe. However, it has not been shown to be effective in the treatment of this disease.

I'll give you a sense of what the efficacy parameters look like. If you go from this is the high-risk population, the PS2s traditionally do poorly with chemotherapy. They do more poorly than their so-called better-risk counterparts, the PS0s and 1s. But, however, paclitaxel and carboplatin together does provide a survival advantage of about 4.7 months. However, the toxicities with that doublet are pretty severe. About half of these patients will develop a grade IV toxicity. And as such, paclitaxel and carboplatin doublets, or so-called PS2s, predominantly remain in academic treatment centers as opposed to in the community. You can see that single-agent paclitaxel is relatively weak as an agent in this disease, two and a half months median survival. That's ten weeks. And as I said, Gemcitabine, most people would now argue

that Gemcitabine probably has no activity in this disease. The recent study looking at standard versus high dosing PS2s show that the median survival is 60 days, both low and high dose. So, clearly probably not an active agent in the treatment of lung cancer, specifically the PS2s.

We did a phase II study in about 30 patients. About a third were PS2s. They were all elderly, and the median age of this group was 76, which is quite an advanced age for this population. And what got us encouraged and the thought leaders encouraged, again, the powerability. Half of these patients received four or more cycles. That's three months or more of therapy, with a third receiving five months or more of therapy. And, in fact, if you look at the overall survival in this group, the median (inaudible) estimates were just about 5.4 months. That's 22 weeks for the PS2s. And amongst the zeros and ones, it was 8.8 months. So, we took single-agent 175 paclitaxel and had, albeit in a small cohort, results that looked as good or better than double therapy in this population.

And that really the side effect profile will be put up. You had one patient that had neutropenia and grade IV neutropenia out of the group, and that actually this is a comparison. If you look at the incidence of grade IV neutropenia between Taxotere, Taxol, XYOTAX and Gemcitabine, you can see at 175 XYOTAX about 9% of patients will get grade IV versus 27% for pac at the standard dose of docetaxel is about half of these patients. And you can see that we have, like Taxol has, an increasing incidence of grade IV neutropenia as you go up in dose. However, it is significantly less than what you see with paclitaxel. But we recently lowered the dose in our STELLAR 4 study really based upon this observation. We took it down from 235 down to 175, and the rationale being that that the Gemcitabine arm, you'd expect only 6% to have grade IV neutropenia. We would expect about 27% in the paclitaxel arm to do that. That may have contributed to some early i.e., the four or five neutropenic events that we're seeing in the first and second cycles. At 175, we know that it's an effective dose from our phase II data, and we believe that it will be as well-tolerated. Clearly, it's the more activation paclitaxel has been Gemcitabine, and we're pretty confident that this study has a high likelihood of success.

These are our three STELLAR studies. STELLAR 2 is certainly the largest of the three, and that's the second-line treatment versus Taxotere. That study is going extremely well from an enrollment perspective. We have forecasted late next June for enrollment completion. STELLAR 3, we've forecasted for the end of December for its completion. In fact, I think we're going to be well ahead of schedule on completing STELLAR 3. And STELLAR 4, even though we stopped enrollment to amend the protocol, enrollment is now back open again, and they've been averaging somewhere between 30 and 50 patients a week in that study. So, again, I don't think we will have any issues with enrollment or timelines.



I'm just going to wrap it up by talking a little bit about ovarian cancer, a different disease and different problems. The main issue with ovarian cancer is toxicity. If you look at Taxol, carboplatin is very effective in this disease. About 30% to 40% will have complete remissions. If you give them maintenance Taxol, you can actually improve their time of disease progression by almost a year. The big issue with Taxol in this setting is the majority of patients require dose reductions because of the toxicity. So, it's really a quality-of-life and a toxicity issue.

This was data that was presented at ECCO, and this is a compilation of 44 patients in our XYOTAX platinum studies. And we broke it out by, there were a number of patients that had ovarian cancer in this phase I trial. The drug was extremely well-tolerated in combination with platinum. You can see that patients received anywhere between 2 and 12 cycles, a median of 9 for the responders and 4 for those patients that had just stable disease. A very active regimen. Most importantly, even in platinum and taxane resistant or refractory disease, this drug had significant anti-tumor activity. This is the single-agent therapy that actually is going to be published in *JCO* early next year. And, again, single-agent activity both in sensitive and resistant disease in patients who have failed one or two prior regimens, very attractive response rates, and again, those responses were durable.

This is the toxicity profile that we like to refer to, single-agent 175, heavily pretreated patients, a 2% instance of grade IV neutropenia, no hair loss, no significant side effects. In neuropathy of about 11% is what you would see with Taxol, but remember, in this study these patients had anywhere between 4 and 12 prior regimens.

The GOG is actively discussing with the FDA, as we speak, a design for a proposal that we think is a sure win. If the FDA signs off on that study design, we think that this will be a very low-risk route for registration in an ovarian cancer setting, and we'll look forward to updating you on that. As Matt said, we expect data out on the first STELLAR study late next summer, as we have forecasted, in our first NDA, which is a fast track rolling submission. We anticipate the clinical section to be completed late in the fourth quarter of next year.

Over the next three to six months, again, a lot of work going on with the regulatory agencies, specifically really starting the GOG phase III ovarian trial and actually providing some more visibility about what that study is. Completing the enrollment for our XYOTAX phase III lung program, and then starting up the Pixantrone phase III study in aggressive lymphoma, as well as we have some other surprises on the TRISENOX® front as well. You're going to see a number of key presentations certainly at ASH this year, as we put out this morning with the 25 presentations on TRISENOX® alone.

We look forward to updating you on that product, and obviously completing our merger with Novuspharma and making Pixantrone a very exciting story going forward as well.

Thank you for your time and attention. We do have a breakout session in one of the breakout rooms.

\*\*\*

#### CAUTIONARY STATEMENT REGARDING FORWARD LOOKING STATEMENTS

This transcript 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 transcript 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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.