CELL THERAPEUTICS INC
Form 10-K
March 08, 2012
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2011

OR

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission file number: 001-12465

CELL THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Washington	**91-1533912**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
501 Elliott Avenue West, Suite 400	
Seattle, WA 98119	**98119**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code: (206) 282-7100

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, no par value	**The NASDAQ Stock Market LLC**
Preferred Stock Purchase Rights	**None**

Securities registered pursuant to Section 12(g) of the Act:

None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of the registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨(Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No x

As of June 30, 2011, the aggregate market value of the registrant s common equity held by non-affiliates was $262,221,235. Shares of common stock held by each executive officer and director and by each person known to the registrant who beneficially owns more than 5% of the outstanding shares of the registrant s common stock have been excluded in that such persons may under certain circumstances be deemed to be affiliates. This determination of executive officer or affiliate status is not necessarily a conclusive determination for other purposes. The registrant has no non-voting common stock outstanding.

The number of outstanding shares of the registrant s common stock as of March 2, 2012 was 226,608,687.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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Forward Looking Statements

This Annual Report on Form 10-K and the documents incorporated by reference may contain, in addition to historical information, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. These statements relate to our future plans, objectives, expectations, intentions and financial performance, and assumptions that underlie these statements. All statements other than statements of historical fact are forward-looking statements for the purposes of these provisions, including:

- any statements regarding future operations, plans, regulatory filings or approvals;
- any statement regarding the performance, or likely performance, or outcomes or economic benefit of any licensing or other agreement, including any agreement with Novartis International Pharmaceutical Ltd., or Novartis, or its affiliates, including whether or not such partner will elect to participate, terminate or otherwise make elections under any such agreement or whether any regulatory authorizations required to enable such agreement will be obtained;
- any projections of cash resources, revenues, operating expenses or other financial terms;
- any statements of the plans and objectives of management for future operations or programs;
- any statements concerning proposed new products or services;
- any statements on plans regarding proposed or potential clinical trials or new drug filing strategies or timelines;
- any statements regarding compliance with the listing standards of The NASDAQ Stock Market, or NASDAQ;
- any statements regarding pending or future mergers or acquisitions; and
- any statement regarding future economic conditions or performance, and any statement of assumption underlying any of the foregoing.

When used in this Annual Report on Form 10-K, terms such as anticipates, believes, continue, could, estimates, expects, intends, may, potential, predicts, should, or will or the negative of those terms or other comparable terms are intended to identify such forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that may cause industry trends or actual results, level of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these statements. Our actual results may differ significantly from the results discussed in such forward-looking statements. These factors include, but are not limited to, those listed under Part I, Item I Business, Item 1A Risk Factors, Item 7 Management s Discussion and Analysis of Financial Condition and Results of Operations, and elsewhere in this Annual Report on Form 10-K.

We do not intend to update any of the forward-looking statements after the date of this Annual Report on Form 10-K to conform these statements to actual results or changes in our expectations. Readers are cautioned not to place undue reliance on these forward-looking statements, which apply only as of the date of this Annual Report on Form 10-K.

You may review a copy of this Annual Report on Form 10-K, including exhibits and any schedule filed therewith, and obtain copies of such materials at prescribed rates, at the U.S. Securities and Exchange Commission s, or the SEC, Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330.

The SEC maintains a website (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding registrants, such as Cell Therapeutics, Inc., that file electronically with the SEC.

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PART I

Item 1. Business

Overview

We develop, acquire and commercialize novel treatments for cancer. Our goal is to build a leading biopharmaceutical company with a diversified portfolio of proprietary oncology drugs. Our research, development, acquisition and in-licensing activities concentrate on identifying and developing new, less toxic and more effective ways to treat cancer. We are currently focusing our efforts on Pixuvri™ (pixantrone dimaleate), or Pixuvri, OPAXIO (paclitaxel poliglumex), or OPAXIO, tosedostat, brostallicin and bisplatinates.

We are developing Pixuvri, a novel anthracycline derivative, for the treatment of hematologic malignancies and solid tumors. Pixuvri was studied in our EXTEND, or PIX301, clinical trial, which is the first randomized, controlled, phase III single-agent clinical trial of Pixuvri for patients with relapsed or refractory aggressive non-Hodgkin s lymphoma, or NHL, who received two or more prior therapies and who were sensitive to treatment with anthracyclines. In the U.S., we initially completed our new drug application, or NDA, submission with the U.S. Food and Drug Administration, or the FDA, in June 2009. In early April 2010, we received a complete response letter from the FDA regarding our NDA for Pixuvri recommending that we design and conduct an additional trial to demonstrate the safety and efficacy of Pixuvri and other items. We filed an appeal in December 2010 with the FDA s Center for Drug Evaluation and Research regarding the FDA s decision in April 2010 to not approve Pixuvri. The appeal was filed under the FDA s formal dispute resolution process asking the Office of New Drugs, or the OND, to conclude that PIX301 demonstrated efficacy.

The FDA responded allowing us to resubmit the NDA with additional information. Prior to resubmitting the NDA, we initiated an additional Pixuvri clinical trial, PIX-R TRIAL, or PIX306, to study Pixuvri in combination with rituximab in patients with relapsed, aggressive NHL that received at least one prior therapy. On October 25, 2011, we announced the resubmission of the NDA to the FDA s Division of Oncology Products 1, or DOP1, for accelerated approval to treat relapsed or refractory aggressive NHL in patients who failed two or more lines of prior therapy. On December 6, 2011, we announced that the FDA s DOP1 had notified us that our resubmitted NDA is considered a complete, Class 2 response to the FDA s April 2010 complete response letter. The FDA set a Prescription Drug User Fee Act, or PDUFA, goal date of April 24, 2012 for a decision on the NDA.

On January 3, 2012, we announced that the FDA s Oncologic Drugs Advisory Committee, or ODAC, was scheduled to review our resubmitted NDA for Pixuvri on February 9, 2012. On January 30, 2012, we announced that we had voluntarily withdrawn our NDA for Pixuvri. The NDA was withdrawn because, after communications with the FDA, we needed additional time to prepare for the review of the NDA by the FDA s ODAC at its February 9, 2012 meeting. Prior to withdrawing the NDA, we requested that the FDA consider rescheduling the review of the NDA to the ODAC meeting to be held in late March. The FDA was unable to accommodate our request to reschedule, and given the April 24, 2012 PDUFA date, the only way to have Pixuvri possibly considered at a later ODAC meeting was to withdraw and later resubmit the NDA. We plan to resubmit the NDA in 2012.

In Europe, we filed a Marketing Authorization Application, or MAA, for commercialization of Pixuvri, which was accepted for review by the European Medicines Agency, or the EMA, in December 2010. On February 17, 2012, Pixuvri was granted a positive opinion for conditional approval from the EMA s Committee for Medicinal Products for Human Use, or CHMP. The CHMP recommended Pixuvri for conditional approval as monotherapy for the treatment of adult patients with multiple relapsed or refractory aggressive non-Hodgkin B-cell lymphomas. The CHMP positive opinion for Pixuvri will now be reviewed by the European Commission, which has the authority to approve medicines for use in the E.U. If the CHMP s recommendation is formally adopted by the European Commission, Pixuvri would be approved for marketing in the 27 countries that are members of the E.U., as well as the European Economic Area. We are hopeful that a conditional marketing authorization for Pixuvri should be granted by the European Commission within the first half of 2012.

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Similar to accelerated approval regulations in the U.S., conditional marketing authorizations are granted to medicinal products with a positive benefit/risk assessment that address unmet medical needs and whose availability would result in a significant public health benefit. A conditional marketing authorization is renewable annually. Under the provisions of the conditional marketing authorization for Pixuvri, we will be required to complete a post-marketing study aimed at confirming the clinical benefit previously observed. The CHMP has accepted PIX306 study as the study to confirm clinical benefit. As a condition of approval, we have agreed to have available the PIX306 clinical trial results by June 2015. We are working with consultants to develop a go-to-market strategy in Europe, including product messaging, positioning, staffing and resources required for Pixuvri product introduction in the E.U. If the European Commission adopts the positive opinion rendered by the CHMP for Pixuvri and if we successfully implement our go-to-market strategy, we expect to begin product launch on an E.U. country-by-country basis beginning in the second half of 2012.

Another late-stage drug candidate of ours, OPAXIO, is being studied as a potential maintenance therapy for women with advanced stage ovarian cancer who achieve a complete remission following first-line therapy with paclitaxel and carboplatin. This phase III study, the GOG0212 trial, is under the control of the Gynecologic Oncology Group, or GOG, and is expected to enroll 1,100 patients with 843 patients enrolled as of December 31, 2011. OPAXIO is also being studied in follow-on phase II trial for the treatment of metastatic brain cancer based on encouraging results from a prior phase II study in this disease.

We are also developing tosedostat in collaboration with Chroma Therapeutics, Ltd., or Chroma. We entered into a co-development and license agreement with Chroma in March 2011, providing us with exclusive marketing and co-development rights to Chroma s drug candidate, tosedostat, in North, Central and South America. Tosedostat is an oral, aminopeptidase inhibitor that has demonstrated significant anti-tumor responses in blood related cancers and solid tumors in phase I-II clinical trials. Interim results from the phase II OPAL study of tosedostat in elderly patients with relapsed or refractory acute myeloid leukemia, or AML, were presented in June 2011 at the 2011 Annual Meeting of the American Society of Clinical Oncology, or ASCO. These results showed that once-daily, oral doses of tosedostat had predictable and manageable toxicities and demonstrated encouraging response rates at the interim evaluation time point including a high-response rate among patients who received prior hypomethylating agents, which are used to treat myelodysplastic syndrome, or MDS, a precursor of AML. Based on these results, and pending discussions with the FDA, we, in collaboration with Chroma, anticipate initiating a phase III study for patients with relapsed or refractory MDS in the second half of 2012.

We are also developing brostallicin, which is a new class of cancer drug a synthetic DNA minor groove binding agent with a unique mechanism of action. Brostallicin is currently in a phase II trial for the treatment of metastatic triple-negative breast cancer. This study is being conducted by the North Central Cancer Treatment Group, or the NCCTG, and is in the process of enrolling patients.

We are also in the early stages of developing a novel dinuclear-platinum complex. There are three platinates currently commercially available (cisplatin, carboplatin, and oxaliplatin), which are first-line agents in ovarian cancer, lung cancer, testicular cancer, and colorectal cancer, as well as a broad variety of other diseases. We are developing the dinuclear-platinum complex CT-47463, which has a different mechanism of action than the platinum compounds currently commercially available and is substantially more active on many preclinical models, including those with resistance to monoplatinates. We have initiated active pharmaceutical ingredient and formulation development as prerequisites to IND enabling activities for bisplatinates. Depending on our resources and priorities, we may choose to discontinue additional pre-IND work or seek to out-license the product to another third party.

We also continue to evaluate additional novel clinical stage compounds to expand our hematologic cancer product pipeline. We are interested in compounds or products that are complementary to our existing pipeline.

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Product Candidates

Our products are focused on addressing key unmet medical needs in the area of oncology. The following table summarizes our key clinical and preclinical programs for our lead product candidates.

Product Candidate	Indications/Intended Use	Phase/Enrollment Status
Pixuvri	Aggressive NHL, > 1 relapse, combination with rituximab (PIX306)	III/open
(pixantrone dimaleate)		
	Aggressive NHL, => 3 relapses, single-agent (PIX301)	III/closed
	Aggressive NHL, front-line, CPOP-R (PIX203)	II/closed
	Metastatic HER2-negative breast cancer (North Central Cancer Treatment Group)	II/closed
OPAXIO	Ovarian cancer, first-line maintenance (GOG0212-Gynecologic Oncology Group)	
(paclitaxel poliglumex)		III/open
	Metastatic brain cancer (Brown University Oncology Group)	II/open
	Head and neck cancer (SUNY Upstate Medical University)	II/open
	Esophageal cancer (Brown University Oncology Group)	II/closed
Tosedostat	Acute Myeloid Leukemia (HOVON)	II/open
	Acute Myeloid Leukemia, relapsed or refractory (OPAL-Chroma)	II/closed
Brostallicin	Metastatic triple-negative breast cancer (North Central Cancer Treatment Group)	II/open
Bisplatinates	Expected to be solid tumors	Preclinical

Oncology Market Overview and Opportunity

Overview. According to the American Cancer Society, or ACS, cancer is the second leading cause of death in the United States, resulting in close to 577,190 deaths annually, or more than 1,500 people per day and approximately 1.6 million new cases of cancer were expected to be diagnosed in 2012 in the United States. The most commonly used methods for treating patients with cancer are surgery, radiation and chemotherapy. Patients usually receive a combination of these treatments depending upon the type and extent of their disease.

Despite recent advances in sequencing the human genome and the introduction of new biologic therapies for the treatment of cancer, almost all patients with advanced cancer will receive chemotherapy at some point during the treatment of their disease. The cornerstone classes of chemotherapy agents include anthracyclines, camptothecins, platinates and taxanes. Unfortunately, there are significant limitations and complications associated with these agents that result in a high rate of treatment failure. The principal limitations of chemotherapy include:

treatment-related toxicities,

inability to selectively target tumor tissue, and

the development of resistance to the cancer-killing effects of chemotherapy.

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Treatment-related toxicities. The majority of current chemotherapy agents kill cancer cells by disrupting the cell division and replication process. Although this mechanism often works in cancer cells, which grow rapidly through cell division, non-cancerous cells are also killed because they too undergo routine cell division. This is especially true for cells that line the mouth, stomach and intestines, hair follicles, blood cells and reproductive cells (sperm and ovum). Because the mechanism by which conventional cancer drugs work is not limited to cancer cells, their use is often accompanied by toxicities. These toxicities limit the effectiveness of cancer drugs and seriously impact the patient s quality of life.

Inability to selectively target tumor tissue. When administered, chemotherapy circulates through the bloodstream, reaching both tumor and normal tissues. Normally dividing tissues are generally as sensitive as tumor cells to the killing effects of chemotherapy, and toxic side effects limit the treatment doses that can be given to patients with cancer.

Chemotherapy resistance. Resistance to the cancer killing effects of conventional chemotherapy is a major impediment to continued effective treatment of cancer. Many cancer patients undergoing chemotherapy ultimately develop resistance to one or more chemotherapy agents and eventually die from their disease. Because many chemotherapies share similar properties, when a tumor develops resistance to a single drug, it may become resistant to many other drugs as well. Drugs that work differently from existing chemotherapies and are less susceptible to the same mechanisms of resistance have consequently begun to play an important role in treating resistant tumors.

We believe developing agents which improve on the cornerstone chemotherapy classes, in addition to novel drugs designed to treat specific types of cancer and cancer patients, fills a significant unmet medical need for cancer patients. Our cancer drug development pipeline includes a modified anthracycline, a taxane, a DNA minor groove binding agent, and a bisplatinate, each of which has the potential to treat a variety of cancer types.

Drug Candidates

Pixuvri

Anthracyclines are one of the most potent classes of anti-cancer agents used in first-line treatment of aggressive NHL, leukemia and breast cancer. For these diseases, anthracycline-containing regimens can often produce long-term cancer remissions and cures. However, the currently marketed anthracyclines can cause severe, permanent and life-threatening cardiac toxicity when administered beyond widely recognized cumulative lifetime doses. This toxicity often prevents repeat use of anthracyclines in patients who relapse after first-line anthracycline treatment. In addition, the cardiac toxicity of anthracyclines prevents their use in combination with other drugs, such as trastuzumab, that can also cause cardiac toxicity. As a result, chemotherapy regimens that do not include anthracyclines often are used for the second-line treatment of aggressive NHL, leukemia and breast cancer.

We are developing Pixuvri, a novel aza-anthracenedione derivative, for the treatment of NHL, and various other hematologic malignancies, and solid tumors. We believe a next-generation anthracycline with ease of administration, greater anti-tumor activity and less cardiac toxicity could gain a significant share of the anthracycline market. We also believe that such a drug could allow repeat therapy in relapsed patients and could allow combination therapy with a broader range of chemotherapies. Pixuvri is being developed to improve the activity and safety in treating cancers usually treated with the anthracycline family of anti-cancer agents. It is a novel DNA major groove binder with an aza-anthracenedione molecular structure, differentiating it from anthracycline chemotherapy agents. Similar to anthracyclines, Pixuvri inhibits topo-isomerase II, but, unlike anthracyclines, rather than interacalation with DNA, Pixuvri hydrogen bonds to and alkylates DNA, thus forming stable DNA adducts with particular specificity for CpG rich, hypermethylated sites. In addition, the structural motifs on anthracycline-like agents are responsible for the generation of oxygen free radicals and the formation of toxic drug-metal complexes have also been modified in Pixuvri to prevent iron binding and perpetuation of

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superoxide production, both of which are the putative mechanism of anthracycline induced acute cardiotoxicity. These novel pharmacologic differences may allow re-introduction of anthracycline-like potency in the treatment of patients who are otherwise at their lifetime recommended doxorubicin exposure.

Pixuvri for relapsed aggressive NHL

NHL is caused by the abnormal proliferation of lymphocytes, which are cells key to the functioning of the immune system. NHL usually originates in lymph nodes and spreads through the lymphatic system. NHL can be broadly classified into two main forms aggressive NHL is a rapidly growing form of the disease that moves into advanced stages much faster than indolent NHL, which progresses more slowly. NHL is the sixth most common type of cancer. The American Cancer Society s most recent estimates are that there will be 70,130 people diagnosed with NHL in the United States and approximately 18,949 people will die from this disease in the United States in 2012. In Europe, the World Health Organization s International Agency for Research on Cancer s 2008 GLOBOCAN database estimates that in the European Union approximately 74,162 people will be diagnosed with NHL and 31,371 are estimated to die from NHL annually.

There are many subtypes of NHL, but aggressive NHL is one of the more common types of NHL and accounts for about 60% of all NHL cases. Initial therapy for aggressive NHL with anthracycline-based combination therapy cures up to 60% of patients. Of the remaining patients, approximately only half will respond to second-line treatment, but few are cured and there is no effective therapy for patients relapsing after or refractory to second-line treatment. There are no drugs approved in the United States for patients with aggressive NHL that relapse after, or are refractory to, second-line treatment.

Pixuvri was studied in our EXTEND, or PIX301, clinical trial, which was a phase III single-agent trial of Pixuvri for patients with relapsed, refractory aggressive NHL who received two or more prior therapies and who were sensitive to treatment with anthracyclines. In November 2008, we announced that this trial achieved the primary efficacy endpoint. We began a rolling NDA submission to the FDA in April 2009 and completed the submission in June 2009.

In 2010, the FDA completed its inspection of the facilities at NerPharMa DS, S.r.l. and NerPharMa, S.r.l. (two independent pharmaceutical manufacturing companies belonging to Nerviano Medical Sciences S.r.l., in Nerviano, Italy). The FDA found both manufacturing sites in compliance and acceptable for continued manufacturing of the drug in early March 2010. NerPharMa, S.r.l. agreed to manufacture our drug product, Pixuvri, which will be used for clinical and commercial supplies.

On March 22, 2010, the FDA s ODAC panel voted unanimously that the clinical trial data was not adequate to support approval of Pixuvri for this patient population. In early April 2010, we received a complete response letter from the FDA regarding our NDA for Pixuvri recommending that we design and conduct an additional trial to demonstrate the safety and efficacy of Pixuvri and other items. We met with the FDA in August 2010 at an end of review meeting at which time the FDA informed us that the Pixuvri Investigational New Drug application, or IND, and NDA were being transferred to the newly-formed Division of Hematology Drug Products, or the DHP. We filed an appeal in December 2010 with the FDA s Center for Drug Evaluation and Research regarding the FDA s decision in April 2010 to not approve Pixuvri for relapsed/refractory aggressive NHL. The appeal filed under the FDA s formal dispute resolution process asked the Office of New Drugs, or the OND, to conclude that PIX301 demonstrated efficacy. In March 2011, we announced that we met with officials of the OND and presented our arguments supporting our belief that the data contained in the NDA are consistent with the conclusion that Pixuvri is effective for its planned use. At the meeting, the OND requested additional analyses related to the EXTEND clinical study which we submitted.

On May 3, 2011, we announced that the OND responded to our December 2010 appeal of the FDA s April 2010 decision to not approve Pixuvri for relapsed or refractory aggressive NHL. In its response, the OND indicated that after considering the data available in the appeal, it does not believe that accelerated approval of

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our NDA is necessarily out of reach based on a single controlled clinical trial, provided that two key matters can be resolved satisfactorily. First, the circumstances of stopping the PIX301 trial early must be resolved to assure that ongoing results assessment were not dictating the decision to stop. Second, ascertainment of the primary endpoint in the PIX301 study must be determined to have been sound and not subject to bias.

The OND also indicated that our request that the OND find that the data in our NDA demonstrate efficacy and return the NDA to the Office of Oncology Drug Products for consideration of safety and other issues was denied because the OND was not able to conclude that efficacy had been demonstrated. However, the OND also did not find that it could be concluded that PIX301 was a failed study, which warranted application of interim analysis statistical thresholds.

On June 14, 2011, we announced that we had met with the FDA s Division of Oncology Drug Products, or DODP, in a meeting that focused on the documents we proposed to provide regarding the circumstances of stopping the enrollment of PIX301 prior to achieving the original planned patient accrual and the make-up of the new radiology expert panel, as well as our plan to address the items noted in the FDA s complete response letter. The DODP confirmed that our NDA would be reviewed within six months from the resubmission of our NDA. On September 28, 2011, we announced that a second independent radiology assessment of response and progression endpoint data from our PIX301 clinical trial of Pixuvri was achieved with statistical significance. We believe this assessment confirmed the statistical robustness of the PIX301 efficacy data that was previously submitted by us to the FDA in our NDA for Pixuvri.

On October 25, 2011, we announced the resubmission of the NDA to the FDA s DOP1 for accelerated approval to treat relapsed or refractory aggressive NHL in patients who failed two or more lines of prior therapy. On December 6, 2011, we announced that the DOP1 had notified us that our resubmitted NDA is considered a complete, Class 2 response to the FDA s April 2010 complete response letter. The FDA set a PDUFA goal date of April 24, 2012 for a decision on our resubmitted NDA.

On January 3, 2012, we announced that ODAC was scheduled to review our resubmitted NDA for Pixuvri on February 9, 2012. On January 30, 2012, we announced that we had voluntarily withdrawn our resubmitted NDA for Pixuvri. The NDA was withdrawn because, after communications with the FDA, we needed additional time to prepare for the review of the NDA by ODAC at its February 9, 2012 meeting. Prior to withdrawing the NDA, we requested that the FDA consider rescheduling the review of the NDA to the ODAC meeting to be held in late March. The FDA was unable to accommodate our request to reschedule, and given the April 24, 2012 PDUFA date, the only way to have Pixuvri possibly considered at a later ODAC meeting was to withdraw and later resubmit the NDA. We plan to resubmit the NDA in 2012.

We believe the results of the EXTEND trial met its primary endpoint and showed that patients randomized to treatment with Pixuvri achieved a significantly higher rate of confirmed and unconfirmed complete response compared to patients treated with standard chemotherapy had a significantly increased overall response rate and experienced a statistically significant improvement in median progression free survival. Pixuvri had predictable and manageable toxicities when administered at the proposed dose and schedule in the EXTEND clinical trial in heavily pre-treated patients. The most common (incidence greater than or equal to 10%) grade 3/4 adverse events reported for Pixuvri-treated subjects across studies were neutropenia and leukopenia. Other common adverse events (any grade) included infection, anemia, thrombocytopenia, asthenia, pyrexia and cough. Overall, the incidence of grade 3 or greater cardiac adverse events was 7% (five patients) on the Pixuvri arm and 2% (one patient) on the comparator arm. There were an equal number of deaths due to an adverse event in both the Pixuvri and comparator arm.

In March 2011, we initiated the PIX-R trial to study Pixuvri in combination with rituximab in patients with relapsed/refractory diffuse large B-cell lymphoma, or DLBCL. The trial will compare a combination of Pixuvri plus rituximab to a combination of gemcitabine plus rituximab in patients with relapsed or refractory DLBCL

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who have received one to three prior lines of therapy. The PIX-R trial utilizes overall survival, or OS, as the primary endpoint of the study, with a secondary endpoint of progression free survival, or PFS. The PIX-R trial is targeting to enroll approximately 350 patients and will include patients who have failed at least one line of previous therapy and patients who are not candidates for myeloablative chemotherapy and stem cell transplant. We had discussions with the DHP relating to a Special Protocol Assessment, or SPA, and following these discussions we determined that we would not pursue a SPA. The DHP noted that we could conduct a study utilizing PFS along with OS as co-primary endpoints which would be an acceptable design outside of the formal SPA process. At the initiation of the study, co-primary endpoints of OS and PFS were used. Subsequently, an amendment was made to the study protocol in January 2012, to make OS the sole primary endpoint, and PFS a secondary endpoint. As this study is being conducted without a SPA, regulatory acceptability will depend on the magnitude of the difference between the trial study arms as well as a risk and benefit analysis. This study could serve as either a post-approval confirmatory study, if Pixuvri were to be approved on the basis of an NDA that will be re-submitted later in 2012, or as a registration study for approval in the United States.

In Europe in July 2009, we were notified by the EMA that Pixuvri was eligible to be submitted for an MAA through the EMA s centralized procedure. The centralized review process provides for a single coordinated review for approval of pharmaceutical products that is conducted by the EMA on behalf of all European Union, or EU, member states. The EMA also designated Pixuvri as a New Active Substance, or NAS; if approved by the EMA, compounds designated as an NAS are eligible to receive a 10-year market exclusivity period in EU member states. In September 2009, we applied to the EMA for orphan drug designation for Pixuvri, which was granted in December 2009. In September 2009, we also submitted a Pediatric Investigation Plan, or PIP, to the EMA as part of the required filing process for approval of Pixuvri for treating relapsed, refractory aggressive NHL in Europe. In April 2010, the EMA recommended that we submit an updated PIP for Pixuvri following discussions with us about the preclinical and clinical Pixuvri data, including EXTEND, and the desire to explore the potential benefits Pixuvri may offer to children with lymphoid malignancies and solid tumors. We submitted an expanded PIP to the Pediatric Committee of the EMA, or PDCO, in July 2010. The expanded PIP was accepted for review by the PDCO in August 2010. On October 19, 2010, we announced that the PDCO had adopted an opinion agreeing to our PIP. The PDCO also recommended deferral of the initiation of the clinical studies until after Pixuvri receives EMA approval. In November 2010, the MAA seeking approval for Pixuvri for the treatment of adult patients with multiple relapsed or refractory aggressive NHL was validated and accepted for review by the EMA. Since Pixuvri was initially granted orphan drug status by the EMA for the treatment of DLBCL, we agreed to withdraw the orphan designation from the EU register in November 2010 based on the expansion of the MAA to the broader aggressive NHL population.

In June 2010, the Italian Medicines Agency, or AIFA, the national authority responsible for drug regulation in Italy, approved the facility at NerPharMa DS, S.r.l. for the production of Pixuvri drug substance. In July 2010, we signed a supply agreement with NerPharMa, S.r.l. for Pixuvri drug product manufacturing. The five-year contract provides for both the commercial and clinical supply of Pixuvri drug product.

In March 2011, we received the Day 120 list of questions from the EMA s CHMP. In April 2011, we met with the co-rapporteurs and members of the EMA to discuss our proposed responses. Based on feedback and recommendation from the rapporteurs, in order to allow time for preclinical reports to be available, we requested and were granted an extension so that our responses could address the questions in the Day 120 list. In August 2011, we submitted our response to the Day 120 questions. On December 5, 2011, we announced that we had received the Day 180 list of outstanding issues from the EMA s CHMP which contained only one remaining major clinical objection to our MAA and items not deemed to be major issues. To address the remaining major objection, the CHMP required that we provide a literature review of mechanisms of rituximab resistance and analyses that demonstrate the efficacy of Pixuvri in patients with prior rituximab treatment. In addition, the CHMP required that we provide information to address some additional questions that were not deemed to be major issues and could be addressed by additional analyses of currently available data. On January 18, 2012, we presented to the CHMP an oral explanation to address outstanding questions raised by some of the member states.

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On February 17, 2012, Pixuvri was granted a positive opinion for conditional approval from the EMA s CHMP. The CHMP recommended Pixuvri for conditional approval as monotherapy for the treatment of adult patients with multiple relapsed or refractory aggressive non-Hodgkin B-cell lymphomas. The CHMP positive opinion for Pixuvri will now be reviewed by the European Commission, which has the authority to approve medicines for use in the E.U. If the CHMP s recommendation is formally adopted by the European Commission, Pixuvri would be approved for marketing in the 27 countries that are members of the E.U., as well as the European Economic Area. We are hopeful that a conditional marketing authorization for Pixuvri should be granted by the European Commission within the first half of 2012.

Similar to accelerated approval regulations in the U.S., conditional marketing authorizations are granted to medicinal products with a positive benefit/risk assessment that address unmet medical needs and whose availability would result in a significant public health benefit. A conditional marketing authorization is renewable annually. Under the provisions of the conditional marketing authorization for Pixuvri, we will be required to complete a post-marketing study aimed at confirming the clinical benefit previously observed. The CHMP has accepted PIX306 study as the study to confirm clinical benefit. As a condition of approval, we have agreed to have available the PIX306 clinical trial results by June 2015.

Pixuvri for metastatic breast cancer

Pixuvri has also been studied in patients with HER2-negative metastatic breast cancer who have tumor progression after at least two, but not more than three, prior chemotherapy regimens. In the second quarter of 2010, the NCCTG opened this phase II study for enrollment. The study is closed to accrual and results are expected to be reported by the NCCTG later in 2012.

OPAXIO

OPAXIO, which we have previously referred to as XYOTAX, is our novel biologically-enhanced chemotherapeutic agent that links paclitaxel to a biodegradable polyglutamate polymer, resulting in a new chemical entity. We are currently focusing our development of OPAXIO on ovarian, brain, esophageal, head and neck cancer.

OPAXIO was designed to improve the delivery of paclitaxel to tumor tissue while protecting normal tissue from toxic side effects. Unlike vessels in healthy tissue, those in tumor tissue have openings that make them porous. Due to the larger size of OPAXIO compared to standard paclitaxel, OPAXIO leaks through the pores in tumor blood vessels and is preferentially trapped and distributed to the tumor tissue. Once in the tumor tissue, OPAXIO is taken up by the tumor cells through a cellular process called endocytosis. Because the biopolymer OPAXIO is made up of biodigestible amino acids, it is slowly metabolized by lysosomal enzymes (principally cathepsin B) inside the lysosome of the tumor cell. This metabolism releases the active chemotherapy agent, which is paclitaxel. The activity of this enzyme, and thus the rate of release of OPAXIO, is increased in the presence of estrogen.

Because the polymer is water-soluble, OPAXIO can be administered without solvents and other routine pre-medications (such as steroids and antihistamines) generally used to prevent severe allergic reactions, and can be infused over an average of 10 to 20 minutes. Treatment does not affect the patient s ability to drive themselves to and from their treatment centers. OPAXIO remains stable in the bloodstream for several days after administration; this prolonged circulation allows the passive accumulation of OPAXIO in tumor tissue.

Taxanes, including paclitaxel (Taxol®) and docetaxel (Taxotere®), currently are widely used for the treatment of various solid tumors, including non-small cell lung, ovarian, breast and prostate cancers. Paclitaxel is considered a standard-of-care in lung and ovarian cancers, where it is most widely used. Because taxanes are small, hydrophobic agents, their therapeutic potential is limited by unfavorable pharmacokinetic properties. Solvents (such as Cremaphor) are needed for administration, and these solvents are often extremely irritating to blood vessels, requiring surgical placement of a large catheter for administration and a minimum of three hours

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for infusion. They also can cause severe life threatening allergic reactions that typically require pre-medications with steroids and antihistamines. Patients usually require transportation to and from their treatment location. Taxanes exhibit high peak levels of drug immediately following administration that expose normal tissues to toxic effects. Rapid elimination of the drug from blood limits tumor exposure.

The distribution and metabolism of OPAXIO to tumor tissue and subsequent release of active paclitaxel chemotherapy appears to be enhanced by estrogen, potentially allowing for superior effectiveness in women with pre-menopausal estrogen levels. This gender-targeted benefit could also be exploited in post-menopausal women or men through estrogen supplementation.

OPAXIO for ovarian cancer

We are currently focusing our development of OPAXIO as a potential maintenance therapy for women with advanced stage ovarian cancer who achieve a complete remission following first-line therapy with paclitaxel and carboplatin. In April 2004, we announced that we entered into a clinical trial agreement with the GOG to perform a phase III trial, or the GOG0212 trial. We have been advised that the GOG submitted both an IND, which cross references our IND, and a SPA for the GOG0212 trial to the FDA. As such, the GOG0212 trial is conducted and managed by the GOG. The trial is expected to enroll 1,100 patients with 843 patients enrolled as of December 31, 2011. On February 21, 2012, we were informed that the Data Monitoring Committee for GOG0212 adopted an amendment to the study s statistical analysis plan, or SAP, to perform four interim analyses instead of the previously-planned single interim analysis allowing for an earlier analysis of survival results than previously noted. The first interim analysis is expected to take place when 109, versus the previously-planned 138, events occur in the control arm. There are early stopping criteria for either success or futility. The final fifth analysis would be conducted when 301, versus the previously-planned 277, events have occurred in the control arm. We understand that the GOG will attempt to amend its SPA following a discussion with the FDA. Based on feedback from the GOG, the GOG Data Monitoring Committee currently plans to conduct its first interim analysis of overall survival in 2013. If successful, we could utilize those results to form the basis of an NDA for OPAXIO.

OPAXIO for brain cancer

In November 2010, results were presented by the Brown University Oncology Group from a phase II trial of OPAXIO combined with temozolomide, or TMZ, and radiotherapy in patients with newly-diagnosed, high-grade gliomas, a type of brain cancer. The trial demonstrated a high rate of complete and partial responses and an encouragingly high rate of six month PFS. Based on these results, the Brown University Oncology Group has initiated a randomized, multicenter, phase II study of OPAXIO and standard radiotherapy versus TMZ and radiotherapy for newly diagnosed patients with glioblastoma with an active gene termed MGMT that reduces responsiveness to TMZ. The trial goals are to estimate disease free and overall survival for the two study arms.

OPAXIO for esophageal cancer

In June 2009, we announced that, in a study released from Brown University at the 2009 ASCO Annual Meeting, patients with cancer of the lower esophagus had evidence of a high pathological complete response rate when given OPAXIO in addition to cisplatin and full-course radiotherapy. In this phase II clinical trial study, data suggests that OPAXIO may provide enhanced radiation sensitization as compared to standard therapy.

OPAXIO for head and neck cancer

A phase I/II study of OPAXIO combined with radiotherapy and cisplatin was initiated by SUNY Upstate Medical University, in patients with locally advanced head and neck cancer. The results are expected to be presented in late 2012.

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Tosedostat

In March 2011, we entered into a co-development and license agreement with Chroma, providing us with exclusive marketing and co-development rights to Chroma s drug candidate, tosedostat, in North, Central and South America. Tosedostat is an oral, aminopeptidase inhibitor that has demonstrated significant anti-tumor responses in blood related cancers and solid tumors in phase I-II clinical trials. Interim results from the phase II OPAL study of tosedostat in elderly patients with relapsed or refractory AML were presented in June 2011 at the 2011 ASCO Annual Meeting. These results showed that once-daily, oral doses of tosedostat had predictable and manageable toxicities and results demonstrated encouraging response rates including a high-response rate among patients who received prior hypomethylating agents, which are used to treat myelodysplastic syndrome, or MDS, a precursor of AML. Based on these results, and pending discussions with the FDA, we, in collaboration with Chroma, anticipate initiating a phase III study for patients with relapsed or refractory MDS in the second half of 2012.

Brostallicin

We are developing brostallicin through our wholly-owned subsidiary, Systems Medicine LLC, which holds worldwide rights to use, develop, import and export brostallicin. Brostallicin is a synthetic DNA minor groove binding agent that has demonstrated anti-tumor activity and a favorable safety profile in clinical trials in which more than 230 patients have been treated to date. We use a genomic-based platform to guide the development of brostallicin.

In the second quarter of 2010, the NCCTG opened for enrollment a phase II study of brostallicin in combination with cisplatin in patients with metastatic triple-negative breast cancer, or mTNBC. mTNBC is defined by tumors lacking expression of estrogen, progesterone receptors and without over-expression of HER2. Women with mTNBC have very limited effective treatments and, based on the novel mechanism of action of brostallicin and the recognized activity of cisplatin in this disease, the combination of the two agents will be explored by the NCCTG. In addition to standard clinical efficacy measures, biological endpoints will also be evaluated to assist in understanding the specific activity of brostallicin in this disease.

A phase II study of brostallicin in relapsed, refractory soft tissue sarcoma met its predefined activity and safety hurdles and resulted in a first-line phase II clinical trial study that was conducted by the European Organization for Research and Treatment of Cancer, or EORTC. Planned enrollment for this study was completed in August 2008 and the EORTC conducted final data analysis in 2009. The data was reported at the ASCO Annual Meeting in June 2010. The EORTC trial demonstrated, in this hard-to-treat patient group, a modest level of clinical activity with an acceptable level of toxicity. No further development is planned in this indication.

Research and Preclinical Development

Platinates are an important class of chemotherapy agents used to treat a wide variety of cancers. There are three platinates currently commercially available (cisplatin, carboplatin, and oxaliplatin), which are first-line agents in ovarian cancer, lung cancer, testicular cancer, and colorectal cancer, as well as a broad variety of other diseases. We are developing the dinuclear-platinum complex CT-47463. CT-47463 has a different mechanism of action than the commercially available platinum compounds and is substantially more active on many preclinical models including those with resistance to monoplatinates. We have initiated active pharmaceutical ingredient and formulation development as prerequisites to IND enabling activities for bisplatinates. Depending on our resources and priorities, we may choose to discontinue additional pre-IND work or seek to out-license the product to another third party.

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Zevalin (Ibritumomab Tiuxetan)

In March 2009, we divested our interest in the radiopharmaceutical product Zevalin® (ibritumomab tiuxetan), or Zevalin, by selling our 50% interest in the Zevalin joint venture, RIT Oncology, LLC, or RIT Oncology, to Spectrum Pharmaceuticals, Inc., or Spectrum, for $16.5 million. Previously, in December 2008, we closed our transaction with Spectrum to form RIT Oncology, to commercialize and develop Zevalin in the United States. We originally acquired the U.S. rights to develop, market and sell Zevalin from Biogen Idec Inc., or Biogen, in December 2007. We received an initial payment of $6.5 million in gross proceeds from Spectrum in March 2009, $0.8 million of which was used to pay a consent fee to Biogen, and an additional $6.5 million in gross proceeds in April 2009. The remaining $3.5 million we expected to receive from Spectrum, subject to certain adjustments, was disputed and was ultimately released to Spectrum based on the outcome of an arbitration hearing held in May 2009. In addition, as part of the divestiture transaction, we agreed to forego the right to receive up to $15 million in product sales milestone payments in connection with the original transaction establishing the joint venture.

Research and Development Costs

Research and development is essential to our business. We spent $34.9 million, $27.0 million and $30.2 million in 2011, 2010, and 2009, respectively, on company-sponsored research and development activities. Because of the risks and uncertainties associated with the development of a product candidate, we cannot accurately predict when or whether we will successfully complete the development of our product candidates or the ultimate product development cost. Specific comments for individual product candidates are below.

Pixuvri. Pixuvri is an aza-anthracenedione that has distinct structural and physiochemical properties that make its anti-tumor unique in this class of agents. The novel pharmacologic differences between Pixuvri and the other agents in the class may allow re-introduction of anthracycline-like potency in the treatment of patients who are otherwise at their lifetime recommended doxorubicin exposure. We are unable to provide the nature, timing, and estimated costs of the efforts necessary to complete the development of Pixuvri because, among other reasons, we cannot predict with any certainty the pace of enrollment of our clinical trials. Even after a clinical trial is enrolled, preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval and advancement of this compound through the development process. For these reasons, among others, we cannot estimate the date on which clinical development of Pixuvri will be completed or when we will be able to begin commercializing Pixuvri to generate material net cash inflows.

OPAXIO. OPAXIO is our novel biologically enhanced chemotherapeutic agent that links paclitaxel to a biodegradable polyglutamate polymer, resulting in a new chemical entity. We are currently focusing our development of OPAXIO on ovarian, brain, esophageal, head and neck cancer. We are unable to provide the nature, timing, and estimated costs of the efforts necessary to complete the development of OPAXIO because, among other reasons, a third party is conducting the key clinical trial of OPAXIO and even after a clinical trial has been enrolled, preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval and advancement of this compound through the development process. For these reasons, among others, we cannot estimate the date on which clinical development of OPAXIO will be completed or when we will be able to begin commercializing OPAXIO to generate material net cash inflows.

Tosedostat. Tosedostat is an oral, aminopeptidase inhibitor that has demonstrated significant anti-tumor responses in blood related cancers and solid tumors in phase I-II clinical trials. We are unable to provide the nature, timing, and estimated costs of the efforts necessary to complete the development of tosedostat because, among other reasons, we cannot predict with any certainty the pace of enrollment of our clinical trials. Even after a clinical trial is enrolled, preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval and advancement of this compound through the development process. For these reasons, among others, we cannot estimate the date on which clinical development of tosedostat will be completed or when we will be able to begin commercializing tosedostat to generate material net cash inflows.

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Brostallicin. Brostallicin is a synthetic DNA minor groove binding agent that has demonstrated anti-tumor activity. The NCCTG is conducting a phase II study of brostallicin in combination with cisplatin in patients with mTNBC. We are unable to provide the nature, timing, and estimated costs of the efforts necessary to complete the development of brostallicin because, among other reasons, a third party is conducting the clinical trial of brostallicin for which enrollment is subject to their control and even after a clinical trial has been enrolled, preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval and advancement of this compound through the development process. For these reasons, among others, we cannot estimate the date on which clinical development of brostallicin will be completed or when we will be able to begin commercializing brostallicin to generate material net cash inflows.

Bisplatinates (CT-47463). Cisplatin is a platinum-based chemotherapy drug used to treat a wide variety of cancers. We are developing new analogues of the dinuclear-platinum complex, or CT-47463, that we expect may be more potent than cisplatin. CT-47463 is endowed with a unique mechanism of action, active in preclinical studies on a large panel of tumor models, sensitive and refractory to cisplatin, and has a safety profile comparable to that of cisplatin. The novel bisplatinum analogues are rationally designed and synthesized to have improved biopharmaceutical properties that reduce the intrinsic reactivity of the molecule and that demonstrate preclinical anti-tumor efficacy in solid tumor models. We are unable to provide the nature, timing, and estimated costs of the efforts necessary to complete the development of CT-47463 because, among other reasons, a third party is conducting the preclinical trial for CT-47463, no clinical trial design for CT-47463 has been developed yet and even after a clinical trial is enrolled, preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval and advancement of this compound through the development process. For these reasons, among others, we cannot estimate the date on which clinical development of CT-47463 will be completed or when we will be able to begin commercializing CT-47463 to generate material net cash inflows.

The risks and uncertainties associated with completing development on schedule and the consequences to operations, financial position and liquidity if the project is not completed timely are discussed in more detail in the following risk factors, which begin on page 21 of this Form 10-K: *Our financial condition may be harmed if third parties default in the performance of contractual obligations.* ; *We may be delayed, limited or precluded from obtaining regulatory approval of OPAXIO as a maintenance therapy for advanced-stage ovarian cancer and as a radiation sensitizer.* ; *We are subject to extensive government regulation.* ; *Even if our drug candidates are successful in clinical trials, we may not be able to successfully commercialize them.* ; *If we do not successfully develop our product candidates into marketable products, we may be unable to generate significant revenue or become profitable.* ; and *We may take longer to complete our clinical trials than we expect, or we may not be able to complete them at all.*

License Agreements and Additional Milestone Activities

Chroma Therapeutics, Ltd.

We have an agreement with Chroma, or the Chroma Agreement, under which we have an exclusive license to certain technology and intellectual property controlled by Chroma to develop and commercialize the drug candidate, tosedostat, in North, Central and South America, or the Licensed Territory. Pursuant to the terms of the Chroma Agreement, we paid Chroma an upfront fee of $5.0 million upon execution of the agreement and will make a milestone payment of $5.0 million upon the initiation of the first pivotal trial, which could commence in the second half of 2012. The Chroma Agreement also includes additional development- and sales-based milestone payments related to AML and certain other indications, up to a maximum amount of $209.0 million payable by us to Chroma if all development and sales milestones are achieved.

We will also pay Chroma royalties on net sales of tosedostat in any country within the Licensed Territory, commencing on the first commercial sale of tosedostat in any country in the Licensed Territory and continuing with respect to that country until the later of (a) the expiration date of the last patent claim covering tosedostat in

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that country, (b) the expiration of all regulatory exclusivity periods for tosedostat in that country or (c) ten years after the first commercial sale in that country. Royalty payments to Chroma are based on net sales volumes in any country within the Licensed Territory and range from the low- to mid-teens as a percentage of net sales.

We will oversee and be responsible for performing the development operations and commercialization activities in the Licensed Territory and Chroma will oversee and be responsible for performing the development operations and commercialization activities worldwide except for the Licensed Territory, or the ROW Territory. Development costs may not exceed $50.0 million for the first three years of the Chroma Agreement unless agreed by the parties and we will be responsible for 75% of all development costs, while Chroma will be responsible for 25% of all development costs, subject to certain exceptions. Chroma is responsible for the manufacturing of tosedostat for development purposes in the Licensed Territory and the ROW Territory in accordance with the terms of the manufacturing and supply agreement. We have the option of obtaining a commercial supply of tosedostat from Chroma or from another manufacturer at our sole discretion in the Licensed Territory. The Chroma Agreement may be terminated by us at our convenience upon 120 days written notice to Chroma. The Chroma Agreement may also be terminated by either party following a material breach by the other party subject to notice and cure periods.

University of Vermont

We have an agreement with the University of Vermont, or UVM, which grants us an exclusive license, with the right to sublicense, for the rights to pixantrone, or the UVM Agreement. Pursuant to the UVM Agreement, we acquired the rights to make, have made, sell and use pixantrone. Pursuant to the UVM Agreement, we are obligated to make payments to UVM based on net sales. Our royalty payments range from low-single digits to mid-single digits as a percentage of net sales. The higher royalty rate is payable for net sales in countries where specified UVM licensed patents exist, or where we have obtained orphan drug protection, until such UVM patents or such protection no longer exists. For a period of ten years after first commercialization of pixantrone, the lower royalty rate is payable for net sales in such countries after expiration of the designated UVM patents or loss of orphan drug protection, and in all other countries without such specified UVM patents or orphan drug protection. Unless otherwise terminated, the term of the UVM Agreement continues for the life of the licensed patents in those countries in which a licensed patent exists, and continues for ten years after the first sale of pixantrone in those countries where no such patents exist. We may terminate the UVM Agreement, on a country-by-country basis or on a patent-by-patent basis, at any time upon advance written notice. UVM may terminate the UVM Agreement upon advance written notice in the event royalty payments are not made. In addition, either par