CELL THERAPEUTICS INC
Form 10-K
March 04, 2014
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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, 2013

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)**
3101 Western Avenue, Suite 600	
Seattle, WA	**98121**
(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**

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

Preferred Stock Purchase Rights

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. ¨

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 28, 2013, the aggregate market value of the registrant s common equity held by non-affiliates was $106,673,063. 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 February 24, 2014 was 149,637,666.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement relating to its 2014 annual meeting of shareholders, or the 2014 Proxy Statement, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The 2014 Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

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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, as amended, 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;
- any projections of revenues, operating expenses or other financial terms, and any projections of cash resources, including regarding our potential receipt of future milestone payments under any of our agreements with third parties;
- 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 partnerships, 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 1, Business, Part I, Item 1A, Risk Factors, Part II, 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.

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PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the acquisition, development and commercialization of less toxic and more effective ways to treat cancer. Our goal is to build a profitable company by generating income from products we develop and commercialize, either alone or with partners. We are currently concentrating our efforts on treatments that target blood-related cancers where there is an unmet medical need. We are primarily focused on commercializing PIXUVRI® (pixantrone) in the European Union, or the E.U., for multiply relapsed or refractory aggressive non-Hodgkin lymphoma, or NHL, and conducting a Phase 3 clinical trial program of pacritinib for the treatment of myelofibrosis that will support regulatory submission for approval in the United States, or the U.S., and Europe.

PIXUVRI

PIXUVRI is a novel aza-anthracenedione derivative that is structurally related to anthracyclines and anthracenediones, but does not appear to be associated with the same level of cardiotoxic effects. In May 2012, the European Commission granted conditional marketing authorization in the E.U. of PIXUVRI as a monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive NHL, a cancer caused by the abnormal proliferation of lymphocytes, which are cells that are key to the functioning of the immune system. NHL usually originates in lymph nodes and spreads through the lymphatic system. PIXUVRI is the first approved treatment in the E.U. for patients with multiply relapsed or refractory aggressive B-cell NHL who have failed two or three prior lines of therapy. This approval was based on the results from our pivotal Phase 3 clinical trial known as EXTEND or PIX301. In connection with the conditional marketing authorization, we are conducting a required post-approval commitment trial, which compares pixantrone and rituximab with gemcitabine and rituximab in the setting of aggressive B-cell NHL.

During the fourth quarter of 2012, we began making PIXUVRI available to healthcare providers in certain countries in the E.U. and initiated our commercial operations on a country-by-country basis. As of the date of this filing, PIXUVRI was available in Austria, Denmark, Finland, Germany, Italy, France, Netherlands, Norway, Sweden and the United Kingdom, or the U.K. We have established a commercial organization, including sales, marketing and supply chain management, to commercialize PIXUVRI in the E.U. PIXUVRI is not approved in the U.S. We are pursuing potential partners for commercializing PIXUVRI in additional markets within the E.U. and other markets outside the E.U. and the U.S.

In almost all European markets, pricing and availability of prescription pharmaceuticals are subject to governmental control. Decisions by governmental authorities will impact the price and market acceptance of PIXUVRI. Accordingly, any future revenues are dependent on market acceptance of PIXUVRI, the reimbursement decisions made by the governmental authorities in each country where PIXUVRI is available for sale and other factors. In the third quarter of 2013, PIXUVRI was granted market access in Italy and France. In December 2013, we reached agreement for funding and reimbursement with the National Association of Statutory Health Insurance Funds, or the GKV-Spitzenverband, in Germany. In February 2014, the National Institute for Health and Care Excellence, or NICE, issued final guidance recommending the prescription of PIXUVRI for as long as we make the Patient Access Scheme, or PAS, available. The PAS is a confidential pricing and access agreement with the U.K. s Department of Health. As a result of these decisions, PIXUVRI is reimbursed under varying conditions in Italy, France, Germany and England/Wales.

Pacritinib

In May 2012, we expanded our late-stage pipeline of product candidates with the acquisition of pacritinib, an oral inhibitor of both Janus Kinase 2, or JAK2, and FMS-like tyrosine kinase, or FLT3, which demonstrated meaningful clinical benefits and good tolerability in myelofibrosis patients in Phase 2 clinical trials. Myelofibrosis is a blood-related cancer caused by the accumulation of malignant bone marrow cells that triggers

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an inflammatory response, scarring the bone marrow and limiting its ability to produce red blood cells prompting the spleen and liver to take over this function. Symptoms that arise from this disease include enlargement of the spleen, anemia, extreme fatigue, itching and pain. We believe pacritinib may offer an advantage over other JAK inhibitors through effective relief of symptoms with less treatment-emergent thrombocytopenia and anemia.

In November 2013, we entered into a worldwide license agreement, or the Baxter Agreement, with Baxter International, Inc., or Baxter, to develop and commercialize pacritinib. Pursuant to the Baxter Agreement, we have joint commercialization rights with Baxter for pacritinib in the U.S., while Baxter has exclusive commercialization rights for all indications outside the U.S. Under the terms of the Baxter Agreement, we received a $60 million upfront payment, which included an equity investment of $30 million, and we have the potential to receive $302 million in clinical, regulatory, commercial launch and sales milestones. Additionally, if pacritinib is approved and launched, we will share U.S. profits equally and will receive royalties on net sales of pacritinib in non-U.S. markets. For additional information relating to the Baxter Agreement, see Part I, Item 1, Business License Agreements and Additional Milestones Baxter .

As part of our collaboration with Baxter, we are pursuing a broad approach to advancing pacritinib for patients with myelofibrosis by conducting two Phase 3 clinical trials: one in a broad set of patients without limitations on blood platelet counts, the PERSIST-1 trial, which was initiated in January 2013; and the other in patients with low platelet counts, the PERSIST-2 trial, which opened for enrollment in March 2014. In October 2013, we reached an agreement with the U.S. Food and Drug Administration, or FDA, on a Special Protocol Assessment, or SPA, for PERSIST-2. This trial, together with PERSIST-1, is intended to support registration in the U.S. and the E.U.

Other Pipeline Candidates

Our earlier stage product candidate, tosedostat, is an oral aminopeptidase inhibitor that has demonstrated significant responses in patients with acute myeloid leukemia, or AML. It is currently being evaluated in several Phase 2 trials, which are being conducted as cooperative group sponsored and investigator-sponsored trials, or ISTs. These trials are evaluating tosedostat in combination with hypomethylating agents, or HMAs, in AML and myelodysplastic syndrome, or MDS, which are cancers of the blood and bone marrow. We anticipate that data from these signal-finding trials may be used to determine the appropriate design for a Phase 3 trial.

Although our efforts are focused on developing and commercializing treatments that target blood-related cancers, we continue to evaluate our pipeline candidate Opaxio (paclitaxel poliglumex), or Opaxio, which targets solid tumors. We are evaluating this candidate through cooperative group sponsored trials and ISTs, such as the ongoing maintenance therapy trial in patients with ovarian cancer. In addition, we continue to evaluate our other drug candidate, brostallicin.

Our Strategy

Our strategy is to become a leader in the acquisition, development and commercialization of novel therapeutics for the treatment of blood-related cancers. The key elements of our strategy are to:

Successfully Commercialize PIXUVRI. Our key commercial objective is to continue our efforts to build a successful PIXUVRI franchise in Europe. PIXUVRI is currently available in Austria, Denmark, Finland, Germany, Italy, France, Netherlands, Norway, Sweden and the U.K., and we seek to expand the availability of PIXUVRI into additional geographic markets outside the E.U. and the U.S. through potential partnerships in 2014. We are currently focused on educating physicians on the unmet medical need and building brand awareness for PIXUVRI among physicians in the countries where PIXUVRI is currently available. We have achieved reimbursement decisions in England/Wales, France, Germany and Italy, and will continue to seek reimbursement in smaller territories in Western and Northern Europe in 2014.

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Develop Pacritinib in Myelofibrosis and Additional Indications. Together with Baxter, we expect to develop and commercialize pacritinib for patients with myelofibrosis. Our development program for pacritinib includes two Phase 3 registration trials in patients with myelofibrosis, and we expect to report topline data from the first Phase 3 trial in the second half of 2014. Although our efforts are focused on myelofibrosis, we are currently evaluating pacritinib in AML through an ongoing IST and intend to evaluate it in other blood cancers in the future.

Continue to Develop our Other Pipeline Programs. We believe that it is important to maintain a diverse pipeline to sustain our future growth. To accomplish this, we continue to advance the development of our other novel, clinical-stage product candidates, particularly tosedostat and Opaxio, through cooperative group sponsored trials and ISTs. Sponsoring such trials provides us with a more economical approach for further developing our investigational products.

Enter into Product Collaborations to Accelerate Development and Commercialization. We intend to continue to pursue additional collaborations to broaden and accelerate clinical trial development and potential commercialization of our product candidates. Collaborations have the potential to generate non-equity based operating capital, supplement our own internal expertise and provide us with access to the marketing, sales and distribution capabilities of our collaborators in specific territories.

Identify and Acquire Additional Pipeline Opportunities. Our current pipeline is the result of licensing and acquiring assets that we believe were initially undervalued opportunities. We plan to continue to seek out additional product candidates in an opportunistic manner.

Product and Product Candidate Portfolio

The following table summarizes our development pipeline for PIXUVRI, pacritinib and our other late-stage product candidates as to which we have ongoing trials:

Name of Product or Product Candidate(1)	Indications/Intended Use	Status
PIXUVRI	Multiply relapsed or refractory aggressive NHL	Conditional Approval-Marketed in E.U.
(pixantrone dimaleate)	Aggressive NHL, 2nd line > 1 relapse, combination with rituximab (PIX306) post-approval study	Phase 3 ongoing
Pacritinib	Myelofibrosis, PERSIST-1, All platelet levels	Phase 3 ongoing
	Myelofibrosis, PERSIST-2, Platelet counts £100,000/µL	Phase 3 initiated(4)
	Relapsed AML	Phase 2 ongoing
Tosedostat(2)	First-line AML	Phase 2 ongoing
	Relapsed/Refractory AML/MDS(3)	Phase 2 ongoing
Opaxio(2)	Ovarian cancer, first-line maintenance (3)	Phase 3 ongoing
(paclitaxel poliglumex)	Newly diagnosed glioblastoma without MGMT methylation	Phase 2 ongoing
	Head and neck cancer	Phase 2 ongoing

(1) Our product candidate portfolio also includes brostallicin, a novel, synthetic, second-generation DNA minor groove binder. See Part I, Item 1, Business Development Candidates Brostallicin for additional information.
(2) We support the development of these investigational agents through cooperative group sponsored trials and ISTs.
(3) These trials have completed enrollment and the patients are being followed.
(4) This trial opened for enrollment in March 2014.

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Oncology Market Overview and Opportunity

Overview. According to the American Cancer Society, or ACS, cancer is the second leading cause of death in the U.S., resulting in close to 580,350 deaths annually, or more than 1,600 people per day. Approximately 1.7 million new cases of cancer were expected to be diagnosed in 2013 in the U.S. 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.

We believe developing agents that improve on the cornerstone chemotherapy classes, in addition to novel drugs designed to target biological pathways to treat specific types of cancer and cancer patients, fills a significant unmet medical need for cancer patients.

Commercialized Product

PIXUVRI

Overview

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 that can also cause cardiac toxicity. As a result, chemotherapy regimens that do not include anthracyclines are often used for the second-line treatment of aggressive NHL, leukemia and breast cancer.

PIXUVRI is being developed in an effort to improve the activity and safety in treating cancers often treated with the anthracycline family of anti-cancer agents. PIXUVRI is not an anthracycline and is instead a novel aza-anthracenedione with unique structural and physiochemical properties. Based on its ease of administration, anti-tumor activity and reduced risk of cardiotoxicity, we believe PIXUVRI 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. Unlike the anthracyclines, PIXUVRI does not inhibit topo-isomerase II. Also 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. This results in progressive disruption of mitosis and therefore killing of rapidly dividing cells like those found in many tumors. 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 superoxide production, both of which are the putative mechanism of anthracycline induced acute cardiotoxicity. These novel pharmacologic differences may allow re-introduction of a single-agent chemotherapy drug with anthracycline-like potency in the treatment of patients who are otherwise at their lifetime recommended doxorubicin exposure.

PIXUVRI for the Treatment of NHL

We are specifically developing and commercializing PIXUVRI for the treatment of 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. The ACS estimated that there would be 69,740 people diagnosed with NHL in the U.S. and approximately 19,020 people would die from this disease in 2013. In Europe, the World Health Organization s International Agency for Research on Cancer s 2008 GLOBOCAN database estimates that in the E.U. approximately 79,312 people will be diagnosed with NHL and 30,691 are estimated to die from NHL annually. NHL is the seventh most common type of cancer. NHL can be broadly classified into two main forms, each with many subtypes aggressive NHL is a rapidly growing form of the disease that moves into advanced stages much faster than indolent NHL, which progresses more slowly.

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There are many types and subtypes of NHL, although aggressive B-cell NHL is the most common and accounts for about 50 percent of NHL cases. After initial therapy for aggressive NHL with anthracycline-based combination therapy, one-third of patients typically develop progressive diseases. Approximately half of these patients are likely to be eligible for intensive second-line treatment and stem cell transplantation, although 50 percent are expected not to respond. For those patients who fail to respond or relapse following second-line treatment, treatment options are limited and usually palliative. PIXUVRI is the first treatment approved in the E.U. for treatment of patients with multiply relapsed or refractory aggressive B-cell NHL. There are no drugs approved for this indication in the U.S.

Clinical Trials and Conditional Marketing Approval of PIXUVRI in the E.U.

The pivotal Phase 3 EXTEND, or PIX301, trial evaluated PIXUVRI for patients with relapsed or refractory aggressive NHL. The trial enrolled 140 patients randomized to receive either PIXUVRI or another single-agent drug currently used for the treatment of this patient population and selected by the physician. Twenty percent of patients in the trial who received pixantrone achieved a complete or unconfirmed complete response at end of treatment compared with 5.7 percent in the comparator group (p=0.021). Median progression-free survival, or PFS, in the intent-to-treat population was also greater with pixantrone than with comparators: 5.3 versus 2.6 months (p=0.005). PIXUVRI had predictable and manageable toxicities when administered at the proposed dose and schedule in heavily pre-treated patients. The most common (incidence greater than or equal to 10 percent) grade 3/4 adverse events reported for PIXUVRI-treated subjects across trials 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 percent (five patients) on the PIXUVRI arm and 2 percent (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. The EXTEND study was published in *Lancet Oncology* in May 2012.

In May 2012, PIXUVRI was granted conditional marketing authorization by the European Commission, or the E.C., as a monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive NHL. The E.C. granted conditional marketing authorization based on the results from the EXTEND pivotal trial.

Similar to accelerated approval regulations in the U.S., conditional marketing authorizations are granted in the E.U. 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 are required to complete a post-marketing study by June 2015 aimed at confirming the clinical benefit previously observed. In this regard, our post-marketing study is an ongoing randomized, controlled Phase 3 clinical trial, known as PIX306, which compares PIXUVRI-rituximab to gemcitabine-rituximab in patients who have relapsed after one to three prior regimens for aggressive B-cell NHL and who are not eligible for autologous stem cell transplant. The PIX306 trial was initiated in March 2011. In December 2013, we gained agreement from the European Medicines Agency, or the EMA, to change the primary endpoint of the PIX306 trial from overall survival to PFS. The trial is now expected to enroll approximately 220 patients versus the 350 patients previously planned. This trial is expected to complete enrollment in 2015 and is intended to support the conversion of the conditional approval for PIXUVRI in Europe to full approval and potentially support a registration application in the U.S.

Commercialization of PIXUVRI in the E.U.

In September 2012, we initiated E.U. commercialization of PIXUVRI and by the end of 2012 made PIXUVRI available to healthcare providers in eight E.U. countries, including Austria, Denmark, Finland, Germany, Netherlands, Norway, Sweden and the U.K. Future revenues are dependent on market acceptance of PIXUVRI, the reimbursement decisions made by the governmental authorities in each country where PIXUVRI is available for sale and other factors.

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In the third quarter of 2013, PIXUVRI was granted market access in Italy and France. In December 2013, we reached agreement for funding and reimbursement with the GKV-Spitzenverband in Germany. In February 2014, NICE issued final guidance recommending the prescription of PIXUVRI for as long as we make the Patient Access Scheme, or PAS, available. The PAS is a confidential pricing and access agreement with the U.K. s Department of Health. We have established distributors in Israel and Turkey for PIXUVRI and through a named patient program in certain countries where the drug is not otherwise commercially available. A named patient program is a mechanism through which physicians can prescribe investigational drugs under individual country-specific guidelines for patients prior to marketing approval.

In July 2012, we entered into an agreement with Quintiles Commercial Europe Limited, or Quintiles, under which we interview, approve for hire, train and manage a sales force and medical science liaisons for PIXUVRI in the E.U. We believe this is a cost effective way to commercialize PIXUVRI in the E.U. We currently have approximately 20 sales and medical science liaisons in the countries where PIXUVRI is reimbursed.

As discussed in Part I, Item 1, Business Manufacturing, Distribution and Associated Matters, we utilize third parties for the manufacture, storage and distribution of PIXUVRI, as well as for other associated supply chain requirements. Our strategy of utilizing third parties in such manner allows us to direct our resources to the development and commercialization of products rather than to the establishment of manufacturing facilities.

Clinical Development of PIXUVRI in the U.S.

Although we are not currently pursuing regulatory approval of PIXUVRI in the U.S., we may reevaluate a possible resubmission strategy in the U.S. based on the data generated from the ongoing PIX306 clinical trial. Previously, in 2009, we had submitted to the FDA a completed New Drug Application, or NDA, submission for PIXUVRI, and, in 2010, the FDA issued a complete response letter. In 2011, we resubmitted 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. In December 2011, the DOP1 notified us that our resubmitted NDA was considered a complete, Class 2 response to the FDA s 2010 complete response letter. The FDA set a Prescription Drug User Fee Act goal date of April 2012 for a decision on our resubmitted NDA. In February 2012, we voluntarily withdrew our resubmitted NDA for PIXUVRI because additional time was required to prepare the necessary information.

Development Candidates

Pacritinib

Pacritinib is an oral tyrosine kinase inhibitor with dual activity against JAK2 and FLT3. The JAK family of enzymes is a central component in signal transduction pathways, which are critical to normal blood cell growth and development as well as inflammatory cytokine expression and immune responses. Mutations in these kinases have been shown to be directly related to the development of a variety of blood-related cancers, including myeloproliferative neoplasms, leukemia and lymphoma. Pacritinib may offer an advantage over other JAK inhibitors through effective treatment of symptoms while having less treatment-emergent thrombocytopenia and anemia than has been seen in currently approved and in-development JAK inhibitors. We acquired pacritinib in May 2012 pursuant to an agreement under which we have certain royalty and milestone payment obligations. See Part I, Item 1, Business License Agreements and Additional Milestone Activities for additional information.

Pacritinib has been studied in two Phase 2 trials with a total of 65 myelofibrosis patients, all of whom were treated with 400 mg of once-daily pacritinib. In December 2013, an integrated analysis of these two Phase 2 trials was presented at the American Society of Hematology Annual Meeting, or ASH. During these Phase 2 trials, spleen response was assessed by physical exam and magnetic resonance imaging, or MRI, and patient-reported outcomes used the Myelofibrosis Symptom Assessment Form, or MF-SAF. Among evaluable patients, 37 percent achieved 35 percent or greater reduction in spleen volume measured by MRI and 48 percent achieved a 50 percent or greater reduction in patient-reported symptom score up to their last visit on treatment. Duration of exposure and daily dose were unaffected by baseline platelet counts. This integrated safety analysis of all 65

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patients showed the most common non-hematologic adverse events (occurring in 15 percent or more of patients overall) were gastrointestinal, predominantly diarrhea, and most were grade 1 or 2, regardless of baseline platelet counts. Of note, there were no thrombocytopenia-associated adverse events occurring at this frequency in either group.

In November 2013, we entered into the Baxter Agreement to develop and commercialize pacritinib. Pursuant to the Baxter Agreement, we have joint commercialization rights with Baxter for pacritinib in the U.S., while Baxter has exclusive commercialization rights for all indications outside the U.S. Under the terms of the Baxter Agreement, we received a $60 million upfront payment, which included an equity investment of $30 million, and we have the potential to receive $302 million in clinical, regulatory, commercial launch and sales milestones. Additionally, if pacritinib is approved and launched, we will share U.S. profits equally and receive royalties on net sales of pacritinib in markets outside of the U.S.

As part of our collaboration with Baxter, we are pursuing a broad approach to advancing pacritinib for patients with myelofibrosis by conducting two Phase 3 clinical trials: one in a broad set of patients without limitations on blood platelet counts, the PERSIST-1 trial, which was initiated in January 2013; and the other in patients with low platelet counts, the PERSIST-2 trial, which opened for enrollment in March 2014.

In January 2013, we initiated clinical trial sites and began enrolling patients with myelofibrosis in a Phase 3 clinical trial known as the PERSIST-1, or PAC325, trial. PERSIST-1 is a multicenter, open-label, randomized, controlled Phase 3 trial evaluating the efficacy and safety of pacritinib with that of best available therapy in patients with primary myelofibrosis. A total of approximately 320 eligible patients are expected to be randomized 2:1 to receive either pacritinib 400 mg taken orally once daily or the best available therapy. Best available therapy includes any physician-selected treatment other than JAK inhibitors, and there is no exclusion by patient platelet count.

The primary endpoint of the PERSIST-1 trial is the percentage of patients achieving a 35 percent or greater reduction in spleen volume from baseline to Week 24 as measured by MRI or computed tomography, or CT, scan. The secondary endpoint is the percentage of patients achieving a 50 percent or greater reduction in Total Symptom Score, or TSS, from baseline to 24 weeks as measured by tracking specific symptoms on a form. At the time of initiation of the trial, PERSIST-1 utilized the original Myeloproliferative Neoplasm Symptom Assessment (MPN-SAF TSS) instrument, to measure TSS reduction. However, we have substantially concluded the process of amending the PERSIST-1 trial protocol to replace the original MPN-SAF TSS instrument with a new instrument, known as the MPN-SAF TSS 2.0, which is also being used for recording patient-reported outcomes for the PERSIST-2 trial detailed below. In connection with this amendment, we expect that enrollment in PERSIST-1 will be increased from 270 to approximately 320 patients. The trial is currently enrolling patients at clinical sites in Europe, Australia, New Zealand, Russia and the U.S. More details on the PERSIST-1 trial can be found at www.clinicaltrials.gov. We anticipate reporting topline data for PERSIST-1 in the second half of 2014.

In March 2014, we opened clinical trial sites for enrollment of patients with myelofibrosis in the second Phase 3 clinical trial known as the PERSIST-2, or PAC326, trial. PERSIST-2 is a multi-center, open-label randomized, controlled clinical trial evaluating pacritinib in up to 300 patients with myelofibrosis whose platelet counts are less than or equal to 100,000/μL. The trial will evaluate pacritinib as compared to best available therapy, including approved JAK2 inhibitors that are dosed according to the product label for myelofibrosis patients with thrombocytopenia. Patients will be randomized (1:1:1) to receive 200 mg pacritinib twice daily, 400 mg pacritinib once daily or best available therapy. In October 2013, CTI reached an agreement with the FDA on a SPA for the PERSIST-2 trial, regarding the planned design, endpoints and statistical analysis approach of the trial to be used in support of a potential NDA submission. Under the SPA, the agreed upon co-primary endpoints are the percentage of patients achieving a 35 percent or greater reduction in spleen volume measured by MRI or CT scan from baseline to 24 weeks of treatment and the percentage of patients achieving a TSS reduction of 50 percent or greater using six key symptoms as measured by the modified MPN-SAF diary from baseline to 24 weeks. The trial is expected to enroll patients at clinical sites in the U.S., Canada, Europe, Australia and New Zealand. Additional trial details are available at www.clinicaltrials.gov.

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Tosedostat

Tosedostat is a selective, oral inhibitor of aminopeptidases, which are required by tumor cells to provide amino acids necessary for growth and tumor cell survival. Tosedostat has demonstrated significant anti-tumor responses in blood-related cancers and solid tumors in Phase 1 and 2 clinical trials.

In December 2011, final results from the Phase 2 OPAL study of tosedostat in elderly patients with relapsed or refractory AML were presented at ASH. These results showed that once-daily, oral doses of tosedostat had predictable and manageable toxicities and demonstrated encouraging response rates, including a high response rate among patients who received prior hypomethylating agents, which are used to treat MDS, a precursor of AML.

In December 2013, interim results from an investigator-initiated Phase 2 clinical trial of tosedostat in combination with cytarabine or decitabine in newly diagnosed older patients with AML or high-risk MDS were presented at ASH. The Phase 2 trial was designed to test the efficacy of tosedostat in combination with low intensity therapy for older patients with previously untreated AML or high-risk MDS not considered candidates for standard intensive therapy. This presentation reported on the results of 26 patients (median age was 69) enrolled in the first dose cohort. Patients were randomized for treatment with tosedostat in combination with either cytarabine or decitabine. Fourteen out of 26 (54 percent) patients in this cohort had either a complete response (CR; n=10, 39 percent) or complete response with incomplete blood count recovery (CRi; n=4, 15 percent). The percentage of complete responses was comparable between arms. Seven (50 percent) of the 14 CR/CRi were achieved in patients with poor-risk cytogenetic features. Importantly, 10 of the 26 patients subsequently went on to receive hematopoietic stem cell transplant. The study achieved its primary objective with 21 (82 percent) patients alive at four months. Median overall survival was encouraging at approximately 12 months for both study arms. Tosedostat combination therapy was well tolerated and predominantly administered as an outpatient therapy. The primary side effects of the combination therapy, the majority of which were associated with the cytarabine arm, included febrile neutropenia (50 percent), pulmonary infections (31 percent) and sepsis (19 percent). Clinically significant non-hematological toxicities were uncommon and predominantly low grade.

There are several ongoing Phase 2 cooperative group sponsored trials and ISTs evaluating the activity of tosedostat in combination with standard agents in patients with AML or MDS. We anticipate that data from these signal-finding trials may inform the appropriate design for a Phase 3 trial.

We have an exclusive marketing and co-development agreement for tosedostat in North, Central and South America, which is discussed in more detail in Part I, Item 1, Business License Agreements and Additional Milestone Activities.

Opaxio (paclitaxel poliglumex)

Opaxio is our novel biologically-enhanced chemotherapeutic agent that links paclitaxel to a biodegradable polyglutamate polymer, resulting in a new chemical entity. Taxanes, including paclitaxel (Taxol®) and docetaxel (Taxotere®), are widely used for the treatment of various solid tumors, including non-small cell lung, ovarian, breast and prostate cancers. We are currently focusing our development of Opaxio through cooperative group trials and ISTs in the following indications: ovarian, glioblastoma multiforme, and head and neck cancers.

Opaxio was designed to deliver paclitaxel preferentially to tumor tissue. By linking paclitaxel to a biodegradable amino acid carrier, the conjugated chemotherapeutic agent is inactive in the bloodstream, sparing normal tissues the toxic side effects of chemotherapy. Once inside tumor tissue, the conjugated chemotherapeutic agent is activated and released by the action of an enzyme called cathepsin B. Opaxio remains stable in the bloodstream for several days after administration; this prolonged circulation allows the passive accumulation of Opaxio in tumor tissue.

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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 March 2004, we entered into a clinical trial agreement with the Gynecologic Oncology Group, or the GOG, to perform a Phase 3 trial, known as the GOG-0212 trial. As such, the GOG-0212 trial is conducted and managed by the GOG. The GOG-0212 study is a randomized, multicenter, open label Phase 3 trial of either monthly Opaxio or paclitaxel for up to 12 consecutive months compared to surveillance among women with advanced ovarian cancer who have no evidence of disease following first-line therapy with paclitaxel and carboplatin. For purposes of registration, the primary endpoint of the study is overall survival of Opaxio compared to surveillance. Secondary endpoints are PFS, safety and quality of life.

In February 2012, we were informed that the Data Monitoring Committee for GOG-0212 adopted an amendment to the study s statistical analysis plan to perform four interim analyses instead of the previously-planned single interim analysis allowing for an earlier analysis of survival results than previously noted. There are early stopping criteria for either success or futility. In January 2013, we were informed that the Data Safety Monitoring Board recommended continuation of the GOG-0212 Phase 3 clinical trial of Opaxio for maintenance therapy in ovarian cancer with no changes following a planned interim survival analysis. In January 2014, we were informed by the GOG that enrollment in the trial had been completed with 1,150 patients enrolled.

Opaxio for glioblastoma multiforme (malignant brain cancer)

In November 2010, results from a Phase 2 trial of Opaxio combined with temozolomide, or TMZ, and radiotherapy in patients with newly-diagnosed, high-grade gliomas, a type of brain cancer, were presented by the Brown University Oncology Group. 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 2 trial 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 primary endpoints of the trial are to estimate disease free and overall survival for the two study arms. Preliminary results are expected to be available in the second quarter of 2014. In September 2012, Opaxio was granted orphan-drug designation by the FDA for the treatment of a type of brain cancer called glioblastoma multiforme.

Opaxio for head and neck cancer

In April 2008, SUNY Upstate Medical University initiated a Phase 1-2 trial of Opaxio combined with radiotherapy and cisplatin for patients with locally advanced head and neck cancer. In June 2013, results from the Phase 1-2 trial showed promising clinical activity and the combination of the two agents was tolerable. An expansion cohort of HPV negative advanced head and neck cancer patients on this protocol is in progress.

We acquired an exclusive worldwide license for rights to Opaxio and certain polymer technology from PG-TXL Company, L.P., or PG-TXL, in November 1998 as discussed below in Part I, Item 1, Business License Agreements and Additional Milestone Activities PG-TXL.

Brostallicin

Brostallicin, a novel, synthetic, second-generation DNA minor groove binder, binds covalently to DNA within the DNA minor groove, interfering with DNA division and leading to tumor cell death. More than 200 patients have been treated with brostallicin in single-agent and combination studies. In June 2013, we reported on final results from a cooperative group sponsored trial and National Cancer Institute-sponsored Phase 2 clinical trial of brostallicin in combination with cisplatin for the treatment of women with metastatic triple-negative breast cancer, or mTNBC. Triple-negative breast cancer lacks progesterone and estrogen receptors and the HER2 biomarker that is present in most breast cancers, which makes standard therapy with hormone or targeted therapy

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ineffective. The rationale for the present study in TNBC is based on data that demonstrates that silencing of the breast cancer susceptibility gene(s), or BRCA, is associated with substantially enhanced sensitivity to brostallicin. BRCA is silenced or mutated in most patients with TNBC. In this study of 48 patients with heavily pretreated mTNBC, the 3-month PFS was 51 percent with 10 confirmed responses (one complete response and nine partial responses). Among the 25 patients who received a reduced brostallicin dose, the overall response rate was 28 percent, with 3-month PFS of 61.5 percent and median overall survival of 11.8 months. Adverse events were mostly hematologic (75 percent) and consistent with other treatments in this setting. The final data were presented at the 2013 American Society for Clinical Oncology Meeting.

We have worldwide rights to use, develop, import and export brostallicin pursuant to a license agreement, which is discussed in more detail in Part I, Item 1, Business License Agreements and Additional Milestone Activities.

Research and Development Expenses

Research and development is essential to our business. We spent $33.6 million, $33.2 million and $34.9 million in 2013, 2012 and 2011, respectively, on company-sponsored research and development activities. The development of a product candidate involves inherent risks and uncertainties, including, among other things, that we cannot predict with any certainty the pace of enrollment of our clinical trials. As a result, we are unable to provide the nature, timing and estimated costs of the efforts necessary to complete the development of pacritinib, tosedostat and Opaxio or to complete the post-approval commitment study of PIXUVRI. Further, third parties are conducting key clinical trials for tosedostat and Opaxio. 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 these product candidates will be completed or when we will generate material net cash inflows from PIXUVRI or be able to begin commercializing, pacritinib, tosedostat and Opaxio to generate material net cash inflows. For additional information relating to our research and development expenses, see Part II, Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations Results of Operations Research and development expenses.

The risks and uncertainties associated with completing development of our product candidates on schedule and the consequences to operations, financial position and liquidity if our research and development projects are not completed timely are discussed in more detail in Part I, Item 1A, Risk Factors.

License Agreements and Additional Milestone Activities

Baxter

In November 2013, we entered into the Baxter Agreement for the development and commercialization of pacritinib for use in oncology and potentially additional therapeutic areas. Under the terms of the Baxter Agreement, we have granted to Baxter an exclusive, worldwide (subject to certain co-promotion rights for us in the U.S.), royalty-bearing, non-transferable, and (under certain circumstances outside of the U.S.) sub-licensable license to our know-how and patents relating to pacritinib. Licensed products under the Baxter Agreement consist of products in which pacritinib is an ingredient.

Baxter has granted to us a non-exclusive license in order for us to perform our rights and obligations under the Baxter Agreement, including our co-promotion rights and manufacturing obligations.

Baxter paid us an upfront payment of $60 million, which included $30 million to acquire 30,000 shares of our convertible preferred stock. In November 2013, Baxter converted such preferred stock into our common stock at an initial conversion price of $1.914 per share.

We are also eligible to receive potential payments of up to $302 million upon the successful achievement of certain development and commercialization milestones, comprised of $112 million of potential clinical,

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regulatory and commercial launch milestone payments, and potential additional sales milestone payments of up to $190 million. Of such milestones, $67 million relates to clinical progress milestones. We and Baxter will jointly commercialize and share profits and losses on sales of pacritinib in the U.S.

We will be responsible for all development costs incurred prior to January 1, 2014, as well as for approximately $96 million in U.S. and E.U. development costs incurred on or after January 1, 2014. Of such $96 million in development costs, we anticipate that up to $67 million will be offset through the potential receipt from Baxter through 2015 of the aforementioned clinical progress milestones. All development costs exceeding the $96 million threshold will generally be shared as follows: (i) costs generally applicable worldwide will be shared 75 percent to Baxter and 25 percent to us, (ii) costs applicable to territories exclusive to Baxter will be 100 percent borne by Baxter and (iii) costs applicable exclusively to co-promotion in the U.S. will be shared equally between the parties, subject to certain exceptions.

Outside the U.S., we are eligible to receive tiered high single digit to mid-teen percentage royalty payments based on net sales for myelofibrosis, and higher double digit royalties for other indications, subject to reduction by up to 50 percent if (i) Baxter is required to obtain additional third party licenses, on which it is obligated to pay royalties, to fulfill its obligations under the Baxter Agreement and (ii) in any jurisdiction where there is no longer either regulatory exclusivity or patent protection.

Joint commercialization, manufacturing, development and steering committees with representatives from Baxter and from us will be established pursuant to the Baxter Agreement. The Baxter Agreement will expire when there is no longer any obligation for Baxter to pay royalties to us in any jurisdiction, at which time the licenses granted to Baxter will become perpetual and royalty-free. We or Baxter may terminate the Baxter Agreement prior to its expiration in certain circumstances. Following the one year anniversary of receipt of regulatory approval in Australia, Canada, China, France, Germany, Italy, Japan, Spain, the U.K. or the U.S., we may terminate the Baxter Agreement as to one or more particular countries if Baxter has not undertaken requisite regulatory or commercialization efforts in the applicable country and certain other conditions are met. Baxter may terminate the Baxter Agreement earlier than its expiration in certain circumstances including (i) in the event development costs for myelofibrosis for the period commencing January 1, 2014 are reasonably projected to exceed a specified threshold, (ii) as to some or all countries in the event of commercial failure of the licensed product or (iii) without cause following the one-year anniversary of the effective date of the Baxter Agreement, provided that such termination will have a lead-in period of six months before it becomes effective. Additionally, either party may terminate the Baxter Agreement prior to its expiration in events of force majeure, or the other party s uncured material breach or insolvency. In the event of a termination prior to the expiration date, rights in pacritinib will revert to us.

The Baxter Agreement also requires Baxter and us to negotiate and enter into a Manufacturing and Supply Agreement, which will provide for the manufacture of the licensed products, with an option for Baxter to finish and package encapsulated bulk product, within 180 days of the effective date of the Baxter Agreement.

University of Vermont

We entered into an agreement with the University of Vermont, or UVM, in March 1995, as amended, or the UVM Agreement, which grants us an exclusive license, with the right to sublicense, for the rights to PIXUVRI. Pursuant to the UVM Agreement, we acquired the rights to make, have made, sell and use PIXUVRI, and we are obligated to make royalty payments to UVM ranging 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 PIXUVRI, 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

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which a licensed patent exists, and continues for ten years after the first sale of PIXUVRI 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 party may terminate the UVM Agreement in the event of an uncured material breach of the UVM Agreement by the other party or in the event of bankruptcy of the other party.

*S*BIO*

We acquired the compounds SB1518 (which is referred to as pacritinib) and SB1578, which inhibit JAK2, from S*BIO Pte Ltd, or S*BIO, in May 2012. Under our agreement with S*BIO, we are required to make milestone payments to S*BIO up to an aggregate amount of $132.5 million if certain U.S., E.U. and Japanese regulatory approvals are obtained or if certain worldwide net sales thresholds are met in connection with any pharmaceutical product containing or comprising any compound that we acquired from S*BIO for use for specific diseases, infections or other conditions. At our election, we may pay up to 50 percent of any milestone payments to S*BIO through the issuance of shares of our common stock or shares of our preferred stock convertible into our common stock. In addition, S*BIO will also be entitled to receive royalty payments from us at incremental rates in the low-single digits based on certain worldwide net sales thresholds on a product-by-product and country-by-country basis.

Chroma Therapeutics, Ltd.

We entered into an agreement, or the Chroma License Agreement, with Chroma Therapeutics, Ltd., or Chroma, in March 2011 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 License Agreement, we are required to make a milestone payment to Chroma of $5.0 million upon the initiation of the first pivotal trial. The Chroma License Agreement also includes additional development- and sales-based milestone payments related to acute myeloid leukemia, or 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.

Under the Chroma License Agreement, we are required to pay Chroma royalties on net sales of tosedostat in any country within the Licensed Territory. Royalties commence on the first commercial sale of tosedostat in any country in the Licensed Territory and continue with respect to that country until the latest of the expiration date of the last patent claim, the expiration of all regulatory exclusivity periods for tosedostat in that country or 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.

Under the Chroma License Agreement, we are required to oversee and are responsible for performing the development operations and commercialization activities in the Licensed Territory, and Chroma will oversee and is responsible for performing the development operations and commercialization activities worldwide except for the Licensed Territory. Development costs may not exceed $50.0 million for the first three years of the Chroma License Agreement unless agreed upon by the parties. We will be responsible for 75 percent of all development costs, while Chroma will be responsible for 25 percent of all development costs, subject to certain exceptions. Chroma is responsible for the manufacturing of tosedostat for development purposes in accordance with the terms of our supply agreement with Chroma. 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 License Agreement may be terminated by us at our convenience upon 120 days written notice to Chroma. The Chroma License Agreement may also be terminated by either party following a material breach by the other party subject to notice and cure periods. As discussed in Part I, Item 3, Legal Proceedings, the parties have certain disputes arising under the Chroma License Agreement, although no court proceedings have commenced as of the time of this filing.

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Gynecologic Oncology Group

We entered into an agreement with the GOG in March 2004, as amended, related to the GOG-0212 trial of Opaxio in patients with ovarian cancer, which the GOG is conducting. We recorded a $0.9 million payment due to the GOG based on the 1,100 patient enrollment milestone achieved in the third quarter of 2013. In addition, we may be required to pay up to $1.2 million upon the attainment of certain milestones, as well as other fees under certain circumstances, of which $0.7 million has been recorded as an accrued expense in our Consolidated Financial Statements as of December 31, 2013.

PG-TXL

In November 1998, we entered into an agreement, or the PG-TXL Agreement, with PG-TXL, as amended, which grants us an exclusive worldwide license for the rights to Opaxio and to all potential uses of PG-TXL s polymer technology. Pursuant to the PG-TXL Agreement, we acquired the rights to research, develop, manufacture, market and sell anti-cancer drugs developed using this polymer technology. Pursuant to the PG-TXL Agreement, we are obligated to make payments to PG-TXL upon the achievement of certain development and regulatory milestones of up to $14.4 million. The timing of the remaining milestone payments under the PG-TXL Agreement is based on trial commencements and completions for compounds protected by PG-TXL license rights, and regulatory and marketing approval of those compounds by the FDA and the EMA. Additionally, we are required to make royalty payments to PG-TXL based on net sales. Our royalty payments range from low-single digits to mid-single digits as a percentage of net sales. Unless otherwise terminated, the term of the PG-TXL Agreement continues until no royalties are payable to PG-TXL. We may terminate the PG-TXL Agreement upon advance written notice to PG-TXL in the event issues regarding the safety of the products licensed pursuant to the PG-TXL Agreement arise during development or clinical data obtained reveal a materially adverse tolerability profile for the licensed product in humans, or for any reason upon advance written notice. In addition, either party may terminate the PG-TXL Agreement upon advance written notice in the event certain license fee payments are not made; in the event of an uncured material breach of the respective material obligations and conditions of the PG-TXL Agreement; or in the event of liquidation or bankruptcy of a party.

Novartis

In January 2014, we entered into a termination agreement, or the Termination Agreement, with Novartis International Pharmaceutical Ltd., or Novartis, to reacquire the rights to PIXUVRI and Opaxio, or the Compounds, previously granted to Novartis under our License and Co-Development Agreement with Novartis entered into in September 2006, as amended, or the Original Agreement. Pursuant to the Termination Agreement, the Original Agreement was terminated in its entirety, other than certain customary provisions, including those pertaining to confidentiality and indemnification, which survive termination.

Under the Termination Agreement, we agreed not to transfer, license, sublicense or otherwise grant rights with respect to intellectual property of the Compounds unless the transferee/licensee/sublicensee agrees to be bound by the terms of the Termination Agreement. We also agreed to provide potential payments to Novartis, including a percentage ranging from the low double-digits to the mid-teens, of any consideration received by us or our affiliates in connection with any transfer, license, sublicense or other grant of rights with respect to intellectual property of PIXUVRI or Opaxio, respectively; *provided* that such payments will not exceed certain prescribed ceilings in the low-single digit millions. Novartis is entitled to receive potential payments of up to $16.6 million upon the successful achievement of certain sales milestones of the Compounds. Novartis is also eligible to receive tiered low single-digit percentage royalty payments for the first several hundred million in annual net sales, and ten percent royalty payments thereafter based on annual net sales of each Compound, subject to reduction in the event generic drugs are introduced and sold by a third party, causing the sale of PIXUVRI or Opaxio to fall by a percentage in the high double-digits. To the extent we are required to pay royalties on net sales of Opaxio pursuant to the PG-TXL Agreement, we may credit a percentage of the amount of such royalties paid to those payable to Novartis, subject to certain exceptions. Notwithstanding the foregoing,

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royalty payments for both PIXUVRI and Opaxio are subject to certain minimum floor percentages in the low single-digits.

Nerviano Medical Sciences

Our license agreement with Nerviano Medical Sciences, S.r.l. for brostallicin, dated October 6, 2006, provides for the potential payment by us of up to $80 million in milestone payments based on the achievement of certain product development results. Due to the early stage of development of brostallicin, we cannot make a determination that the milestone payments are reasonably likely to occur at this time.

Cephalon

In June 2005, we entered into an acquisition agreement with Cephalon, Inc., or Cephalon. Cephalon was subsequently acquired by Teva Pharmaceutical Industries Ltd., or Teva. Under the agreement, we have the right to receive up to $100 million in payments upon achievement by Teva of specified sales and development milestones related to TRISENOX. In November 2013, we received a $5 million payment related to achievement of a sales milestone.

Patents and Proprietary Rights

We dedicate significant resources to protecting our intellectual property, which is important to our business. We have filed numerous patent applications in the U.S. and various other countries seeking protection of inventions originating from our research and development, and we have also obtained rights to various patents and patent applications under licenses with third parties and through acquisitions. Patents have been issued on many of these applications. We have pending patent applications or issued patents in the U.S. and foreign countries directed to PIXUVRI, pacritinib, tosedostat, Opaxio, brostallicin and other product candidates. However, the lives of these patents are limited. Patents for the individual products extend for varying periods according to the date of the patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The Opaxio-directed patents will expire on various dates ranging from 2017 through 2018. The pacritinib-directed patents will expire from 2026 through 2029. The PIXUVRI-directed U.S. patents will expire in 2014. The tosedostat-directed U.S. patents will expire in 2017. The brostallicin-directed U.S. patents will expire on various dates ranging between 2017 through 2021. The PIXUVRI-directed patents currently in force in Europe will expire from 2015 through 2023. Some of these European patents are subject to Supplementary Protection Certificates such that the extended patents will expire from 2020 to 2027. Although certain PIXUVRI-directed patents may be subject to possible patent-term extensions that could provide extensions through 2019 in the U.S. and through 2027 in some additional countries in Europe, there can be no guarantee of extensions of PIXUVRI-directed or other patents in other countries. The risks and uncertainties associated with our intellectual property, including our patents, are discussed in more detail in the following risk factors, which begin on page 21 of this Annual Report on Form 10-K: *We hold rights under numerous patents that we have acquired or licensed or that protect inventions originating from our research and development, and the expiration of any one or more of these patents may allow our competitors to copy the inventions that are currently protected. ; If we fail to adequately protect our intellectual property, our competitive position could be harmed. ; Patent litigation is widespread in the biotechnology industry, and any patent litigation could harm our business. ; and We may be unable to obtain or protect our intellectual property rights and we may be liable for infringing upon the intellectual property rights of others, which may cause us to engage in costly litigation and, if unsuccessful, could cause us to pay substantial damages and prohibit us from selling our products.*

Manufacturing, Distribution and Associated Matters

Our manufacturing strategy utilizes third-party contract manufacturers for our products and product candidates. We utilize third-party contractors for raw materials, active pharmaceutical ingredients and finished drug product, as well as for labeling, packaging, storing and distributing our products and product candidates. As

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our business continues to expand, we expect that our manufacturing, distribution and associated requirements will increase correspondingly. One such requirement becoming increasingly important relates to our commercial supply needs; while we currently have a commercial supply arrangement for PIXUVRI, we do not presently have any such arrangement in place for pacritinib (or for our other product candidates). In particular, as we have continued to advance the development of pacritinib and position such product for potential commercialization, procuring a qualified commercial supplier for pacritinib has become an important objective.

Integral to our manufacturing strategy is our quality control and quality assurance program, which includes standard operating procedures and specifications with the goal that our products and product candidates are manufactured in accordance with current Good Manufacturing Practices, or cGMPs, and other applicable global regulations. The cGMP compliance includes strict adherence to regulations for quality control, quality assurance and the maintenance of records and documentation. The manufacturing facilities for products and product candidates must meet cGMP requirements, and with respect to the commercial products, must have acquired FDA, EMA and any other applicable regulatory approval. In this regard, we expect to continue to rely on contract manufacturers to produce sufficient quantities of our products and product candidates in accordance with cGMPs for use in clinical trials and distribution.

We believe our manufacturing strategy of utilizing qualified outside vendors allows us to direct our financial and managerial resources to development and commercialization activities, rather than to the establishment of a manufacturing infrastructure.

Competition

Competition in the pharmaceutical and biotechnology industries is intense. We face competition from a variety of companies focused on developing oncology drugs. We compete with large pharmaceutical companies and with other specialized biotechnology companies. With respect to PIXUVRI, there are no other products approved in the E.U. as monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive NHL; however there are other agents approved to treat aggressive NHL that could be used in this setting, including both branded and generic anthracyclines as well as mitoxantrone. There are also other investigational candidates being tested in aggressive NHL that, if approved, could compete with PIXUVRI.

With respect to our other investigational candidates, if approved, they may face competition from compounds that are currently approved or may be approved in the future. Pacritinib would compete with Incyte, which markets Jakafi®, and potentially other candidates in development that target JAK inhibition to treat cancer. Tosedostat would compete with corporations such as Eisai Inc., which markets Dacogen®; Celgene Corporation, which markets Vidaza®, Revlimid®, and Thalomid®; Genzyme Corporation, which markets Clolar® and new anti-cancer drugs that may be developed and marketed. Opaxio would compete with other taxanes, epothilones, and other cytotoxic agents, which inhibit cancer cells by a mechanism similar to taxanes, or similar products. Such corporations include, among others, Bristol-Myers Squibb Co., which market paclitaxel and generic forms of paclitaxel; Sanofi-Aventis U.S. LLC, which markets docetaxel; Genentech, Inc., Hoffmann-La Roche Inc. and Astellas Pharma US, Inc., which market Tarceva®; Genentech, Inc. and Hoffmann-La Roche Inc., which market Avastin®; Eli Lilly & Company, which markets Alimta®; and Celgene Corporation, which markets Abraxane®.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than us and may be better equipped to develop, manufacture and market products. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of these competitors have products that have been approved or are in development and operate large, well-funded research and development programs.

We expect to encounter significant competition for the principal pharmaceutical products we plan to develop. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before us may achieve a significant competitive advantage if their products work through a similar mechanism as our products and if the approved indications are similar. We do not believe competition is as intense among products that treat cancer through novel delivery or therapeutic mechanisms

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where these mechanisms translate into a clinical advantage in safety and/or efficacy. A number of biotechnology and pharmaceutical companies are developing new products for the treatment of the same diseases being targeted by us. In some instances, such products have already entered late-stage clinical trials or received FDA or EC approval. However, cancer drugs with distinctly different mechanisms of action are often used together in combination for treating cancer, allowing several different products to target the same cancer indication or disease type. Such combination therapy is typically supported by clinical trials that demonstrate the advantage of combination therapy over that of a single-agent treatment.

We believe that our ability to compete successfully will be based on our ability to create and maintain scientifically advanced technology, develop proprietary products, attract and retain scientific personnel, obtain patent or other protection for our products, obtain required regulatory approvals and manufacture and successfully market our products, either alone or through outside parties. We will continue to seek licenses with respect to technology related to our field of interest and may face competition with respect to such efforts. See the risk factor, *We face direct and intense competition from our competitors in the biotechnology and pharmaceutical industries, and we may not compete successfully against them.* in Part I, Item 1A, Risk Factors of this Annual Report on Form 10-K for additional information regarding the risks and uncertainties we face due to competition in our industry.

Government Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing, among other things, of our products are extensively regulated by governmental authorities in the U.S. and other countries.

U.S. Regulation.

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, Public Health Service Act, or PHSA, and their implementing regulations. Failure to comply with applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications or supplemental applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

Drug Approval Process. None of our drugs may be marketed in the U.S. until such drug has received FDA approval. The steps required before a drug may be marketed in the U.S. include:

- preclinical laboratory tests, animal studies and formulation studies;
- submission to the FDA of an Investigational New Drug Application, or an IND, for human clinical testing, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the investigational product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced, tested, and distributed to assess compliance with cGMPs and Good Distribution Practices; and
- FDA review and approval of the NDA.

Preclinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become

effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA

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unless, before that time, the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. The study protocol and informed consent information for study subjects in clinical trials must also be approved by an Institutional Review Board for each institution where the trials will be conducted. Study subjects must sign an informed consent form before participating in a clinical trial. Phase 1 usually involves the initial introduction of the investigational product into people to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase 2 usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage, (ii) identify possible adverse effects and safety risks, and (iii) evaluate preliminarily the efficacy of the product candidate for specific indications. Phase 3 trials usually further evaluate clinical efficacy and test further for safety by using the product candidate in its final form in an expanded patient population. There can be no assurance that Phase 1, Phase 2 or Phase 3 testing will be completed successfully within any specified period of time, if at all. Furthermore, we or the FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The FDA and IND sponsor may agree in writing on the design and size of clinical trials intended to form the primary basis of an effectiveness claim in an NDA application. This process is known as a SPA. These agreements may not be changed after the clinical trials begin, except in limited circumstances. The existence of a SPA, however, does not assure approval of a product candidate.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical trials, together with other detailed information, including information on the manufacture and composition of the investigational product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. The testing and approval process requires substantial time, effort and financial resources. Submission of an NDA requires payment of a substantial review user fee to the FDA. The FDA will review the application and may deem it to be inadequate to support commercial marketing, and we cannot be sure that any approval will be granted on a timely basis, if at all. The FDA may also seek the advice of an advisory committee, typically a panel of clinicians practicing in the field for which the product is intended, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee.

The FDA has various programs, including fast track, priority review and accelerated approval that are intended to expedite or simplify the process for reviewing drugs and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for one or more of these programs are those for serious or life threatening conditions, those with the potential to address unmet medical needs and those that provide meaningful benefit over existing treatments. We cannot be sure that any of our drugs will qualify for any of these programs, or that, if a drug does qualify, the review time will be reduced or the product will be approved.

Before approving a NDA, the FDA usually will inspect the facility or the facilities where the product is manufactured, tested and distributed and will not approve the product unless cGMP compliance is satisfactory. If the FDA evaluates the NDA and the manufacturing facilities as acceptable, the FDA may issue an approval letter, or in some cases, a complete response letter. A complete response letter contains a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the

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FDA s satisfaction, the FDA will issue an approval letter. The approval letter authorizes commercial marketing of the drug for specific indications. As a condition of approval, the FDA may require post-marketing testing and surveillance to monitor the product s safety or efficacy, or impose other post-approval commitment conditions.

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes or making certain additional labeling claims, are subject to further FDA review and approval. Obtaining approval for a new indication generally requires that additional clinical trials be conducted.

Post-Approval Requirements. Holders of an approved NDA are required to: (i) report certain adverse reactions to the FDA, (ii) comply with certain requirements concerning advertising and promotional labeling for their products, and (iii) continue to have quality control and manufacturing procedures conform to cGMP after approval. The FDA periodically inspects the sponsor s records related to safety reporting and/or manufacturing and distribution facilities; this latter effort includes assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the area of production, quality control and distribution to maintain cGMP compliance. We use and will continue to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal of the product from the market.

Marketing of prescription drugs is also subject to significant regulation through federal and state agencies tasked with consumer protection and prevention of medical fraud, waste and abuse. We must comply with restrictions on off-label use promotion, anti-kickback, ongoing clinical trial registration, and limitations on gifts and payments to physicians. In December 2007, we entered into a corporate integrity agreement, or CIA, with the Office of the Inspector General, Health and Human Services, or OIG-HHS, as part of our settlement agreement with the U.S. Attorney s Office, or USAO, for the Western District of Washington arising out of their investigation into certain of our prior marketing practices relating to TRISENOX, which was divested to Cephalon in July 2005. The term of the CIA, and the requirement that we establish a compliance committee and compliance program and adopt a formal code of conduct, expired as of December 22, 2012, however we intend to continue to abide by the Pharmaceutical Research and Manufacturers of America Code and FDA regulations.

Non-U.S. Regulation.

Before our products can be marketed outside of the U.S., they are subject to regulatory approval similar to that required in the U.S., although the requirements governing the conduct of clinical trials, including additional clinical trials that may be required, product licensing, pricing and reimbursement vary widely from country to country. No action can be taken to market any product in a country until an appropriate application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing review period often begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices may not be approved for such product.

In Europe, marketing authorizations may be submitted at a centralized, a decentralized or national level. The centralized procedure is mandatory for the approval of biotechnology products and provides for the grant of a single marketing authorization that is valid in all E.U. members states. Similar to accelerated approval regulations in the U.S., conditional marketing authorizations are granted in the E.U. 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 are required to complete a post-marketing study aimed at confirming the clinical benefit previously observed.

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The approval of new drugs in the E.U. may be achieved using a mutual recognition procedure, which is available at the request of the applicant for all medicinal products that are not subject to the centralized procedure. These procedures apply in the E.U. member states, as well as in Norway and Iceland. Since the E.U. does not have jurisdiction over patient reimbursement or pricing matters in its member states, we are working or planning to work with individual countries on such matters across the region. However, there can be no assurance that our reimbursement strategy will secure reimbursement on a timely basis or at all.

Environmental Regulation

In connection with our research and development activities, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with these laws, regulations and policies in all material respects and have not been required to take any significant action to correct any noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the controlled use of hazardous materials, including, but not limited to, certain hazardous chemicals and radioactive materials. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by federal, state and local regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources. See the risk factor, *Since we use hazardous materials in our business, we may be subject to claims relating to improper handling, storage or disposal of these materials.* in Part I, Item 1A, Risk Factors of this Annual Report on Form 10-K for additional information regarding the risks and uncertainties we face due to the use of hazardous materials we use in our business.

Employees

As of December 31, 2013, we employed 106 individuals in the U.S., including two employees at our majority-owned subsidiary Aequus Biopharma, Inc., and five in Europe. Our U.S. and U.K. employees do not have a collective bargaining agreement. Two employees in Italy are subject to a collective bargaining agreement. We believe our relations with our employees are good.

Information regarding our executive officers is set forth in Part III, Item 10 below, which information is incorporated herein by reference.

Corporate Information

We were incorporated in Washington in 1991. We completed our initial public offering in 1997 and our shares are listed on The NASDAQ Capital Market in the U.S. and the Mercato Telemarico Azionario, or the MTA, in Italy, where our symbol is CTIC. Our principal executive offices are located at 3101 Western Avenue, Suite 600, Seattle, Washington 98121. Our telephone number is (206) 282-7100. Our website address is http://www.celltherapeutics.com. However, information found on our website is not incorporated by reference into this report. CTI , PIXUVRI and Opaxio are our proprietary marks. All other product names, trademarks and trade names referred to in this Form 10-K are the property of their respective owners. We make available free of charge on our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after each is electronically filed with, or furnished to, the U.S. Securities and Exchange Commission, or the SEC.

In addition, you may review a copy of this Annual Report on Form 10-K, including exhibits and any schedule filed herewith, and obtain copies of such materials at prescribed rates, at the SEC s 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, including the Company, that file electronically with the SEC.

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Item 1a. Risk Factors

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. The occurrence of any of the risks described below and elsewhere in this document, including the risk that our actual results may differ materially from those anticipated in these forward-looking statements, could materially adversely affect our business, financial condition, operating results or prospects and the trading price of our securities. Additional risks and uncertainties that we do not presently know or that we currently deem immaterial may also harm our business, financial condition, operating results and prospects and the trading price of our securities.

Factors Affecting Our Operating Results and Financial Condition

We expect that we will need to raise additional financing to develop our business, but additional funds may not be available on acceptable terms, or at all. Any inability to raise required capital when needed could impair our ability to make our contractually obligated payments and harm our liquidity, financial condition, business, operating results and prospects.

We have substantial operating expenses associated with the development of our product candidates and the commercialization of PIXUVRI, and we have significant contractual payment obligations. Our available cash and cash equivalents were $71.6 million as of December 31, 2013. At our currently planned spending rate, we believe that our present financial resources, together with pacritinib milestone payments projected to be earned and received over the course of 2014 and 2015 under our collaboration with Baxter and expected European sales from PIXUVRI, will be sufficient to fund our operations into the third quarter of 2015. Cash forecasts and capital requirements are subject to change as a result of a variety of risks and uncertainties. Changes in manufacturing, clinical trial expenses, any expansion of our sales and marketing organization in Europe and other unplanned business developments may consume capital resources earlier than planned. Additionally, we may not receive the anticipated pacritinib milestone payments or sales from PIXUVRI. Due to these and other factors, our forecast for the period for which we will have sufficient resources to fund our operations, as well as any other operational or business projection we have disclosed, or may, from time to time, disclose, may fail.

We have $15.0 million outstanding under our senior secured term loan agreement. We are required to make monthly interest payments of approximately $158,000, and commencing May 1, 2014 through October 1, 2016, we will be required to make monthly interest plus principal payments in the aggregate amount of approximately $584,000. The loan agreement also requires us to comply with restrictive covenants, including those that limit our operating flexibility and ability to borrow additional funds. A failure to make a required loan payment or an uncured covenant breach could lead to an event of default, and in such case, all amounts then outstanding may become due and payable immediately.

We expect that we will need to acquire additional funds in order to develop our business, including in the event our costs are greater than anticipated or our cash inflow projections fail, or in the event we seek to expand our operations. We may seek to raise such capital through equity or debt financings, partnerships, collaborations, joint ventures, disposition of assets or other sources, but our ability to do so is subject to a number of risks and uncertainties, including:

- our ability to raise capital through the issuance of additional shares of our common stock or convertible securities is restricted by the limited number of our residual authorized shares, the difficulty of obtaining shareholder approval to increase authorized shares, and the restrictive covenants of our senior secured term loan agreement;
- issuance of equity securities or convertible securities will dilute the proportionate ownership of existing shareholders;
- our ability to raise debt capital is limited by our existing senior secured term loan agreement;

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some of such arrangements may require us to relinquish rights to certain assets; and

we may be required to meet additional regulatory requirements, and we may be subject to certain contractual limitations, which may increase our costs and harm our ability to obtain funding.

Additional funding may not be available on favorable terms or at all. If we fail to obtain additional capital when needed, we may be required to delay, scale back or eliminate some or all of our research and development programs, reduce our selling, general and administrative expenses and/or refrain from making our contractually required payments when due, which could harm our business, financial condition, operating results and prospects.

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

We were incorporated in 1991 and have incurred a net operating loss every year since our formation. As of December 31, 2013, we had an accumulated deficit of $1.9 billion. We are pursuing regulatory approvals for PIXUVRI, pacritinib, tosedostat and Opaxio. We will need to continue to conduct research, development, testing and regulatory compliance activities and procure manufacturing and drug supply services, the costs of which, together with projected general and administrative expenses, may result in operating losses for the foreseeable future. There can be no assurances that we will ever achieve profitability.

If our collaboration with Baxter with respect to pacritinib or any other collaboration for our products or product candidates is not successful, or if we are unable to enter into additional collaborations, we may not be able to effectively develop and/or commercialize the applicable product(s), which could have a material adverse effect on our business.

Under the Baxter Agreement, we rely heavily on Baxter to collaborate with us in respect of the development and global commercialization of our lead product candidate, pacritinib. As a result of our dependence on our relationship with Baxter, the eventual success or commercial viability of pacritinib is, to a certain extent, beyond our control. We are subject to a number of specific risks associated with our dependence on our collaborative relationship with Baxter, including: possible disagreements between Baxter and us as to the timing, nature and extent of our development plans, including clinical trials or regulatory approval strategy; changes in personnel at Baxter who are key to the collaboration efforts; any changes in Baxter s business strategy adverse to our interests; and possible disagreements with Baxter regarding ownership of proprietary rights. Furthermore, the contingent financial returns under our collaboration with Baxter depend in large part on the achievement of development and commercialization milestones, plus a share of revenues from any sales. Therefore, our success, and any associated future financial returns to us and our investors, will depend in large in part on the performance of both Baxter and us under the Baxter Agreement.

The continued development of our other product candidates also depends on our ability to enter into and/or maintain collaborations. We have entered into a third-party service provider agreement with Quintiles Commercial Europe Limited, or Quintiles, whereby Quintiles provides a variety of services related to the commercialization of PIXUVRI in Europe. We are also pursuing potential partners for commercializing PIXUVRI in other markets outside of the U.S. and our current target E.U. markets discussed in Part II, Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations. Because we rely on third parties to manufacture, distribute, and market and sell PIXUVRI, we have limited control over the efforts of these third parties, and we may receive less revenue than if we commercialized PIXUVRI ourselves. We are also a party to other agreements with third parties for our product candidates, including an agreement with the GOG, to perform a Phase 3 trial of Opaxio in patients with ovarian cancer.

If we fail to enter into additional collaborative arrangements or to maintain existing or future arrangements and service provider relationships, we may be unable to further develop and commercialize product candidates, generate revenues to grow, sustain our business or achieve profitability, which would harm our business, financial condition, operating results and prospects.

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Our clinical trials may take longer to complete than expected, or they may not be completed at all.

Our business is dependent on our ability, and to the extent applicable, the ability of our collaboration partners and other third parties (such as cooperative groups and ISTs), to successfully undertake extensive clinical testing on humans to demonstrate to the satisfaction of the applicable regulatory authority the safety and efficacy of the product for its intended use. For example, our ability to develop pacritinib depends on the successful completion of two Phase 3 trials, one of which initiated in January 2013 and the second of which opened for enrollment in March 2014. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. Negative or inconclusive results or adverse medical events during a clinical trial could delay, limit or prevent regulatory approval. We forecast the commencement and completion of clinical trials for planning purposes, but actual commencement or completion may take longer than planned or not be completed at all due to a number of reasons, including:

- we may not obtain authorization to permit product candidates that are already in the preclinical development phase to enter the human clinical testing phase;
- the FDA, the EMA or other regulatory authority may object to proposed protocols or could place a partial or full hold on any clinical trial at any time;
- there may be shortages of available product supplies or the materials that are used to manufacture the products or the quality or stability of the product candidates may fall below acceptable standards;
- authorized preclinical or clinical testing may require significantly more time, resources or expertise than originally expected to be necessary;
- clinical testing may not show potential products to be safe and efficacious for the specific indication for which they are tested and, as with many drugs, may fail to demonstrate the desired safety and efficacy characteristics in human clinical trials;
- the results from preclinical studies and early clinical trials may not be indicative of the results that will be obtained in later-stage clinical trials;
- inadequate financing to complete a clinical trial;
- we, or to the extent applicable, our collaboration partners, or regulatory authorities may suspend clinical trials at any time on the basis that the participants are being exposed to unacceptable health risks or for other reasons; and
- the rates of patient recruitment and enrollment of patients who meet trial eligibility criteria may be lower than anticipated as a result of factors, such as the number of patients with the relevant conditions, the nature of the clinical testing, the proximity of patients to clinical testing centers, the eligibility criteria for tests as well as competition with other clinical testing programs involving the same patient profile but different treatments.

In addition, the failure of third parties, including, where applicable, contract research organizations, academic institutions, collaborators, cooperative groups and/or investigator sponsors, to conduct, oversee and monitor clinical trials, as well as to process clinical results, manage test requests and meet applicable standards, can affect the timing and outcome of the applicable trials. In particular, the clinical trials currently underway for tosedostat and Opaxio are being conducted as cooperative group trials and ISTs, and as such, are not under our control.

A delay in, or failure to commence or complete, any present or planned clinical trials, or the need to perform more or larger clinical trials than planned, could result in an increase in development costs, which could harm our ability to commercialize our product candidates, and our business, financial condition, operating results or prospects.

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Products that appear promising in research and development may be delayed or fail to reach later stages of development or the market.

The successful development of anti-cancer drugs and other pharmaceutical products is highly uncertain, and obtaining regulatory approval to market drugs to treat cancer is expensive, difficult and speculative. A number of companies in the pharmaceutical industry, including us, have suffered significant setbacks in advanced clinical trials, even after reporting promising results in earlier trials. For example, our Phase 3 clinical trials for Opaxio for the treatment of non-small cell lung cancer failed to meet their primary endpoints. In addition, in June 2013, the FDA implemented a partial clinical hold on tosedostat, which prevented new patients from entering any ongoing tosedostat clinical trials. This hold was lifted in December 2013.

Products that appear promising in research and development may be delayed or fail to reach later stages of development or the market for several reasons, including:

- preclinical or clinical trial results may show the product to be less effective than desired or to have harmful or problematic side effects;
- failure to receive the necessary U.S. and international regulatory approvals or a delay in receiving such approvals;
- difficulties in formulating the product, scaling the manufacturing process or getting approval for manufacturing;
- manufacturing costs, pricing, reimbursement issues or other factors may make the product uneconomical to commercialize;
- any problem in the production of our products, such as the inability of a supplier to provide raw materials or supplies used to manufacture our products, equipment obsolescence, malfunctions or failures, product quality or contamination problems, or changes in regulatory requirements or standards that require modifications to our manufacturing process;
- the product candidate may not be cost effective compared to alternative treatments; or
- other companies or people have or may have proprietary rights to a product candidate, such as patent rights, and will not let the product candidate be sold on reasonable terms, or at all.

If the development of our product candidates is delayed, our development costs may increase, the product may not reach later stages of development and/or the ability to commercialize our product candidates may be harmed, which could harm our business, financial condition, operating results or prospects.

We or our collaboration partners may not obtain or maintain the regulatory approvals required to commercialize some or all of our products.

We are subject to rigorous and extensive regulation by the FDA in the U.S. and by comparable agencies in other states and countries, including the EMA in the E.U. Pacritinib and all of our other compounds are currently in research or development and, other than conditional marketing authorization for PIXUVRI in the E.U., we have not received marketing approval for these other compounds or FDA marketing approval of PIXUVRI (and we are not currently pursuing FDA marketing approval of PIXUVRI). Information about the status of the regulatory approval of PIXUVRI, pacritinib, tosedostat and Opaxio can be found in Part II, Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations and is incorporated by reference herein. Our products may not be marketed in the U.S. until they have been approved by the FDA and may not be marketed in other countries until they have received approval from the appropriate agencies. Each product candidate requires significant research, development and preclinical testing and extensive clinical investigation before submission of any regulatory application for marketing approval. Obtaining regulatory approval requires substantial time, effort and financial resources, and we may not be able to obtain approval of any of our products on a timely basis, or at all. The number and focus of preclinical and clinical trials that will be

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required for approval by the FDA, the EMA or any other foreign regulatory agency varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address and the regulations applicable to any particular drug candidate. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or preclude regulatory approval. The FDA, the EMA and other foreign regulatory agencies can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to:

- a drug candidate may not be shown to be safe or effective;
- a clinical trial results in negative or inconclusive results or adverse medical events occur during a clinical trial;
- they may not approve the manufacturing process of a drug candidate;
- they may interpret data from pre-clinical and clinical trials in different ways than we do;
- a drug candidate may fail to comply with regulatory requirements; or
- they might change their approval policies or adopt new regulations.

Any delay or failure by us to obtain regulatory approvals of our products could adversely affect the marketing of our products. If our products are not approved quickly enough to provide net revenues to defray our operating expenses, our business, financial condition and operating results will be harmed.

Even if our drug candidates are successful in clinical trials and receive regulatory approvals, we or our collaboration partners may not be able to successfully commercialize them.

Pacritinib, Opaxio and tosedostat are currently in clinical trials; the development and clinical trials of these products may not be successful and, even if they are, such products may never be successfully developed into commercial products. Even if our products are successful in clinical trials or in obtaining other regulatory approvals, our products (even those that have been granted conditional marketing authorization, such as PIXUVRI) may not reach the market for a number of reasons including:

- they may be found ineffective or cause harmful side effects;
- they may be difficult to manufacture on a scale necessary for commercialization;
- they may be uneconomical to produce;
- we may fail to obtain reimbursement amount approvals or pricing that is cost effective for patients as compared to other available forms of treatment;
- they may not compete effectively with existing or future alternatives to our products;

we are unable to sell marketing rights or develop commercial operations;

they may fail to achieve market acceptance; or

we may be precluded from commercialization of our products by proprietary rights of third parties.

In particular, with respect to the future potential commercialization of pacritinib, we will be heavily dependent on our collaboration partner, Baxter. Under the terms of our agreement, Baxter has exclusive commercialization rights for all indications for pacritinib outside the U.S., while Baxter and CTI share commercialization rights in the U.S.

The failure of Baxter (or any other applicable collaboration partner) to fulfill its commercialization obligations with respect to a product, or the occurrence of any of the events itemized in the foregoing list, could adversely affect the commercialization of our products. If we fail to commercialize products or if our future products do not achieve significant market acceptance, we will not likely generate significant revenues or become profitable.

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If users of our products are unable to obtain adequate reimbursement from third party payers, market acceptance of our products may be limited and we may not achieve anticipated revenues.

To the extent our products are successfully introduced to market, they may not be considered cost-effective and third-party or government reimbursement might not be available or sufficient. Governmental and other third-party payors continue to attempt to contain healthcare costs by strictly controlling, directly or indirectly, pricing and reimbursement, and we expect pressures on pricing and reimbursement from both governments and private payers inside and outside the U.S. to continue. In almost all European markets, pricing and choice of prescription pharmaceuticals are subject to governmental control. Therefore, the price of our products and their reimbursement in Europe is and will be determined by national regulatory authorities. A variety of factors are considered in making reimbursement decisions, including whether there is sufficient evidence to show that treatment with the product is more effective than current treatments, that the product represents good value for money for the health service it provides and that treatment with the product works at least as well as currently available treatments. Reimbursement decisions from any of the European markets may impact reimbursement decisions in other European markets. The continuing efforts of government and insurance companies, health maintenance organizations and other payers of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners and the availability of capital.

We may never be able to generate significant product revenues from the sale of PIXUVRI.

We anticipate that, for at least the next several years, our ability to generate revenues and become profitable will depend on the commercial success in Europe of our only marketed product candidate, PIXUVRI. PIXUVRI is not approved for marketing in the U.S. PIXUVRI is available to healthcare providers in certain countries in the E.U. See Part II, Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations for a discussion of the reimbursement status in the applicable E.U. countries. However, our ability to continue to commercialize PIXUVRI in Europe will depend on our ability to obtain an annual renewal of our conditional marketing authorization for PIXUVRI in the E.U. and to timely complete the post-marketing study of PIXUVRI aimed at confirming the clinical benefit previously observed in PIXUVRI. A failure of such study could result in a cessation of commercialization of PIXUVRI in the E.U.

In addition, the successful commercialization of PIXUVRI in the E.U. depends heavily on our ability to obtain and maintain favorable reimbursement rates for users of PIXUVRI, as well as on various additional factors, including, without limitation, our ability to:

- increase and maintain demand for and sales of PIXUVRI in Europe and obtain greater acceptance of PIXUVRI by physicians and patients;
- establish and maintain agreements with wholesalers and distributors on reasonable terms;
- maintain, and enter into additional, commercial manufacturing arrangements with third-parties, cost-effectively manufacture necessary quantities and build distribution, managerial and other capabilities; and
- further develop and maintain a commercial organization to market PIXUVRI.

If we are unable to successfully commercialize PIXUVRI in Europe as planned, our business, financial condition, operating results and prospects could be harmed.

We have in the past received and may in the future receive audit reports with an explanatory paragraph on our consolidated financial statements.

Our independent registered public accounting firm included an explanatory paragraph in its reports on our consolidated financial statements for each of the years ended December 31, 2007 through December 31, 2011 regarding their substantial doubt as to our ability to continue as a going concern. Although our independent registered public accounting firm removed this going concern explanatory paragraph in its report on our

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December 31, 2012 consolidated financial statements, we expect to continue to need to raise additional financing to develop our business and satisfy obligations as they become due. The inclusion of a going concern explanatory paragraph in future years may negatively impact the trading price of our common stock and make it more difficult, time consuming or expensive to obtain necessary financing, and we cannot guarantee that we will not receive such an explanatory paragraph in the future.

We may not be able to maintain our listings on The NASDAQ Capital Market and the MTA in Italy, or trading on these exchanges may otherwise be halted or suspended, which may make it more difficult for investors to sell shares of our common stock.

Maintaining the listing of our common stock on The NASDAQ Capital Market requires that we comply with certain listing requirements. We have in the past and may in the future fail to continue to meet one or more listing requirements. For example, in June 2012, we received a notification from The NASDAQ Stock Market LLC, or NASDAQ, indicating non-compliance with the requirement to maintain a minimum closing bid price of $1.00 per share and that we would be delisted if we did not timely regain compliance. We regained compliance through a reverse stock split in September 2012, but we could fail to meet the continued listing requirements as a result of a decrease in our stock price or otherwise.

If our common stock ceases to be listed for trading on The NASDAQ Capital Market for any reason, it may harm our stock price, increase the volatility of our stock price, decrease the level of trading activity and make it more difficult for investors to buy or sell shares of our common stock. Our failure to maintain a listing on The NASDAQ Capital Market may constitute an event of default under our senior secured term loan and any future indebtedness, which would accelerate the maturity date of such debt or trigger other obligations. In addition, certain institutional investors that are not permitted to own securities of non-listed companies may be required to sell their shares adversely affecting the trading price of our common stock. If we are not listed on The NASDAQ Capital Market or if our public float falls below $75 million, we will be limited in our ability to file new shelf registration statements on SEC Form S-3 and/or to fully use one or more registration statements on SEC Form S-3. We have relied significantly on shelf registration statements on SEC Form S-3 for most of our financings in recent years, so any such limitations may harm our ability to raise the capital we need. Delisting from The NASDAQ Capital Market could also affect our ability to maintain our listing or trading on the MTA. Trading in our common stock has been halted or suspended on both The NASDAQ Capital Market and MTA in the past and may also be halted or suspended in the future due to market or trading conditions at the discretion of The NASDAQ Stock Market LLC, the Commissione Nazionale per le Società e la Borsa, or CONSOB (which is the public authority responsible for regulating the Italian securities markets), or the Borsa Italiana (which ensures the development of the managed markets in Italy). Any halt or suspension in the trading in our common stock may negatively impact the trading price of our common stock.

We may be unable to obtain a quorum for meetings of our shareholders or obtain necessary shareholder approvals and therefore be unable to take certain corporate actions.

Our articles of incorporation require that a quorum, generally consisting of one-third of the outstanding shares of voting stock, be represented in person, by telephone or by proxy in order to transact business at a meeting of our shareholders. In addition, amendments to our articles of incorporation, such as an amendment to increase our authorized capital stock, generally require the approval of a majority of our outstanding shares. Failure to meet a quorum or obtain shareholder approval can prevent us from raising capital through equity financing or otherwise taking certain actions that may be in the best interest of the company and shareholders.

A substantial majority of our common shares are held by Italian institutions and, under Italian laws and regulations, it is difficult to communicate with the beneficial holders of those shares to obtain votes. In 2006, we were unable to obtain a quorum at two scheduled annual meetings. Following that failure to obtain a quorum, we contacted certain depository banks in Italy where significant numbers of shares of our common stock were held and asked them to cooperate by making a book-entry transfer of their share positions at Monte Titoli to their U.S.

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correspondent bank, who would then transfer the shares to an account of the Italian bank at a U.S. broker-dealer that is an affiliate of that bank. Certain of the banks contacted agreed to make the share transfer pursuant to these arrangements as of the record date of the meeting, subject to the relevant beneficial owner being given notice before such record date and taking no action to direct the voting of such shares. Obtaining a quorum and necessary shareholder approvals at shareholder meetings will depend in part upon the willingness of the Italian depository banks to continue participating in the custody transfer arrangements, and we cannot be assured that those banks that have participated in the past will continue to participate in custody transfer arrangements in the future.

As a result of the foregoing, we may be unable to obtain a quorum or shareholder approval of proposals, when needed, at annual or special meetings of shareholders. Even if we are able to obtain a quorum at our shareholder meetings, we may not obtain enough votes to approve matters to be resolved upon at those meetings. For example, a proposal to approve a reverse stock split failed to receive sufficient votes to pass at the March 2009 shareholders meeting. Any failure to obtain a quorum or the requisite vote on a proposal in question could harm us.

We could fail in financing efforts if we fail to receive shareholder approval when needed.

We are required under the NASDAQ Marketplace Rules to obtain shareholder approval for any issuance of additional equity securities that would comprise more than 20 percent of the total shares of our common stock outstanding before the issuance of such securities sold at a discount to the greater of book or market value in an offering that is not deemed to be a public offering by the NASDAQ Marketplace Rules or NASDAQ as well as under certain other circumstances. We have in the past and may in the future issue additional equity securities that would comprise more than 20 percent of the total shares of our common stock outstanding in order to fund our operations. However, we might not be successful in obtaining the required shareholder approval for any future issuance that requires shareholder approval pursuant to the NASDAQ Marketplace Rules, particularly in light of the difficulties we have experienced in obtaining a quorum and holding shareholder meetings discussed above. If we are unable to obtain financing due to shareholder approval difficulties, such failure may harm our ability to continue operations.

We are subject to limitations on our ability to issue additional shares of our common stock or undertake other business initiatives due to Italian regulatory requirements.

Compliance with Italian regulatory requirements may delay additional issuances of our common stock or other business initiatives. Under Italian law, we must publish a registration document, securities note and summary that have to be approved by CONSOB prior to issuing common stock that exceeds, in any twelve-month period, 10 percent of the number of shares of our common stock outstanding at the beginning of that period, subject to certain exceptions. If we are unable to obtain and maintain a registration document, securities note or summary to cover general financing efforts under Italian law, we may be required to raise money using alternative forms of securities. For example, we have in the past issued convertible preferred stock and may in the future issue convertible securities because the common stock resulting from the conversion of such securities, subject to current provisions of European Directive No. 71/2003 and, according to the current interpretations of the Committee of European Securities Regulators, is not subject to the 10 percent limitation imposed by E.U. and Italian law. However, any changes to Italian regulatory requirements, exemptions or interpretations may increase compliance costs or limit our ability to issue securities.

We are subject to Italian regulatory requirements, which could result in administrative and other challenges and additional expenses.

Because our common stock is traded on the MTA, we are required to also comply with the rules and regulations of CONSOB and the Borsa Italiana, which regulate companies listed on Italy s public markets. Compliance with these regulations and responding to periodic information requests from Borsa Italiana and CONSOB requires us to devote additional time and resources to regulatory compliance matters and to incur

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additional expenses of engaging additional outside counsel, accountants and other professional advisors. Actual or alleged failure to comply with Italian regulators can also subject us to regulatory investigations. For more information on current investigations, see the regulatory investigations that are discussed in more detail in Part I, Item 3, Legal Proceedings.

We will incur a variety of costs for and may never realize the anticipated benefits of acquisitions.

We evaluate and acquire assets and technologies from time to time. If appropriate opportunities become available, we may attempt to acquire other businesses and assets that we believe are a strategic fit with our business. The process of negotiating an acquisition and integrating an acquired business and assets may result in operating difficulties and expenditures. In addition, our acquisitions may require significant management attention that would otherwise be available for ongoing development of our business, whether or not any such transaction is ever consummated. Moreover, we may never realize the anticipated benefits of any acquisition. Any acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or amortization expenses related to intangible assets, which could harm our business, financial condition, operating results or prospects.

We may owe additional amounts for value added taxes related to our operations in Europe.

Our European operations are subject to value added tax, or VAT, which is usually applied to all goods and services purchased and sold throughout Europe. The VAT receivable was $5.7 million and $8.1 million as of December 31, 2013 and December 31, 2012, respectively. On April 14, 2009, December 21, 2009 and June 25, 2010, the Italian Tax Authority, or the ITA, issued notices of assessment to Cell Therapeutics Inc. Sede Secondaria, or CTI (Europe), based on the ITA s audit of CTI (Europe) s VAT returns for the years 2003, 2005, 2006 and 2007. The ITA audits concluded that CTI (Europe) did not collect and remit VAT on certain invoices issued to non-Italian clients for services performed by CTI (Europe). The assessments, including interest and penalties, for the years 2003, 2005, 2006 and 2007 are 0.5 million, 5.5 million, 2.5 million and 0.8 million. While we are defending ourselves against the assessments both on procedural grounds and on the merits of the case, there can be no assurances that we will be successful in such defense. Further information pertaining to these cases can be found in Part I, Item 3, Legal Proceedings and is incorporated by reference herein. If the final decision of the Supreme Court is unfavorable to us, or if, in the interim, the ITA were to make a demand for payment and we were to be unsuccessful in suspending collection efforts, we may be requested to pay to the ITA an amount up to 9.4 million (or approximately $12.9 million converted using the currency exchange rate as of December 31, 2013) plus collection fees, notification expenses and additional interest for the period lapsed between the date in which the assessments were issued and the date of effective payment.

Even if our products receive regulatory approval, we will be subject to ongoing obligations and continued regulatory review by the FDA, the EMA and other foreign regulatory agencies, as applicable, and may be subject to additional post-marketing obligations, all of which may result in significant expense and limit commercialization of our products, including PIXUVRI.

Even if our other products receive regulatory approvals, we will be subject to numerous regulations and statutes regulating the manner of selling and obtaining reimbursement for those products. Regulatory approvals that we receive for our products may be subject to limitations on the indicated uses for which the product may be marketed or require potentially costly post-marketing follow-up studies. Even if a product receives regulatory approval, we may not be able to maintain compliance with regulatory requirements, which could result in the product being withdrawn from the market, product seizures, injunctions, regulatory restrictions on our business and sales activities, monetary penalties or criminal prosecution. In addition, PIXUVRI is subject to extensive regulatory requirements regarding its labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping. If the FDA, the EMA or other foreign regulatory agency approves any of our other products, they will also be subject to similar extensive regulatory requirements. The subsequent discovery of previously unknown problems with PIXUVRI or any of our other products, including adverse events of

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unanticipated severity or frequency, or the discovery that adverse effects or unknown toxicities observed in preclinical research or clinical trials that were believed to be minor actually constitute more serious problems, may result in restrictions on the marketing of the product or withdrawal of the drug from the market. If we are not granted full approval of PIXUVRI in the E.U. or we are unable to renew our conditional marketing authorization for PIXUVRI in the E.U., our business, financial condition, operating results and prospects would be harmed.

We cannot predict the outcome of our clinical trial for PIXUVRI or whether our clinical trial for PIXUVRI will serve as either a post-marketing commitment trial or as a pivotal trial.

In March 2011, we initiated a randomized pivotal trial of PIXUVRI for the treatment of relapsed or refractory aggressive B-cell NHL. This clinical trial, referred to as PIX-R, or PIX306, compares a combination of PIXUVRI plus rituximab to a combination of gemcitabine plus rituximab in patients who have relapsed after one to three prior regimens for aggressive B-cell NHL and who are not eligible for autologous stem cell transplant. We cannot predict the outcome of PIX306 or whether PIX306 will serve as either a post-marketing commitment trial or as a pivotal trial. We may not be able to demonstrate the clinical benefit of PIXUVRI in patients who had previously received rituximab or that PIXUVRI is more clinically effective than treatments currently used in clinical practice. We may not be able to complete the PIX306 clinical trial by June 2015 or at all. If we are unable to submit the clinical trial data from PIX306 by June 2015, it may result in the withdrawal of the conditional marketing authorization by the E.U. We may also need to take additional steps to obtain regulatory approval of PIXUVRI. The expense to design and conduct clinical trials are substantial and any additional clinical trials or actions we may need to pursue to obtain approval of PIXUVRI may negatively affect our business, financial condition, operating results or prospects. Failure to meet clinical trial deadlines may also result in the withdrawal of our conditional marketing authorization for PIXUVRI.

We may be subject to fines, penalties, injunctions and other sanctions if we are deemed to be promoting the use of our products for non-FDA-approved, or off-label, uses.

Our business and future growth depend on the development, use and ultimate sale of products that are subject to FDA, EMA and or other regulatory agencies regulation, clearance and approval. Under the U.S. Federal Food, Drug, and Cosmetic Act and other laws, we are prohibited from promoting our products for off-label uses. This means that in the U.S., we may not make claims about the safety or effectiveness of our products and may not proactively discuss or provide information on the use of our products, except as allowed by the FDA.

Government investigations concerning the promotion of off-label uses and related issues are typically expensive, disruptive and burdensome, generate negative publicity and may result in fines or payments of settlement awards. For example, in April 2007, we paid a civil penalty of $10.6 million and entered into a settlement agreement with the USAO for the Western District of Washington arising out of their investigation into certain of our prior marketing practices relating to TRISENOX, which was divested to Cephalon Inc. in July 2005. As part of that settlement agreement and in connection with the acquisition of Zevalin, we also entered into a corporate integrity agreement with the OIG-HHS, which required us to establish a compliance committee and compliance program and adopt a formal code of conduct. If our promotional activities are found to be in violation of applicable law or if we agree to a settlement in connection with an enforcement action, we would likely face significant fines and penalties and would likely be required to substantially change our sales, promotion, grant and educational activities.

A failure to comply with laws and regulations that govern our cross-border conduct, as well as with healthcare fraud and abuse and false claims laws and regulations, could result in substantial penalties and prosecution.

We are subject to risks associated with doing business outside of the U.S., which exposes us to complex foreign and U.S. regulations. For example, we are subject to regulations imposed by the Foreign Corrupt

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Practices Act, or FCPA, and other anti-corruption laws that generally prohibit U.S. companies and their intermediaries from offering, promising, authorizing or making improper payments to foreign government officials for the purpose of obtaining or retaining business. The SEC and U.S. Department of Justice have increased their enforcement activities with respect to the FCPA. Internal control policies and procedures and employee training and compliance programs that we have implemented to deter prohibited practices may not be effective in prohibiting our employees, contractors or agents from violating or circumventing our policies and the law.

In addition, we are subject to various state and federal fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and federal False Claims Act. There are similar laws in other countries. These laws may impact, among other things, the sales, marketing and education programs for our drugs. The federal Anti-Kickback Statute prohibits persons from knowingly and willingly soliciting, offering, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing or arranging for a good or service, for which payment may be made under a federal healthcare program. The federal False Claims Act prohibits persons from knowingly filing, or causing to be filed, a false claim to, or the knowing use of false statements to obtain payment from the federal government. Suits filed under the False Claims Act can be brought by any individual on behalf of the government and such individuals, commonly known as whistleblowers, may share in any amounts paid by the entity to the government in fines or settlement. Many states have also adopted laws similar to the federal Anti-Kickback Statute and False Claims Act.

We are unable to predict whether we could be subject to actions under any of the foregoing or similar laws and regulations, or the impact of such actions. If we were to be found to be in violation of these laws or regulations, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare reimbursement programs and the curtailment or restructuring of our operations, all of which could have a material adverse effect on our business and results of operations.

We are dependent on third-parties for the manufacture, testing and distribution of products and product candidates. Any failure or delay in manufacturing, or in obtaining a qualified vendor when needed, could delay the clinical development and commercialization of the applicable product(s) and product candidate(s) and harm our business.

We do not currently have internal analytical laboratory or manufacturing facilities to allow the testing or production and distribution of drug products in compliance with cGMPs, and we instead utilize third party vendors. In particular, we are dependent on a single vendor for the manufacturing of each of PIXUVRI, pacritinib and tosedostat. With respect to Opaxio, we are presently relying on stored inventory of the drug, as we do not presently have a manufacturing agreement in place for Opaxio. Because we do not have a manufacturing infrastructure, we are dependent upon our vendors to supply us in a timely manner with products manufactured in compliance with cGMPs or similar manufacturing standards imposed by the U.S. and/or applicable foreign regulatory authorities, including the FDA and EMA. Any of such regulatory authorities may take action against a contract manufacturer who violates cGMPs. Failure of our manufacturers to comply with FDA, EMA or other applicable regulations may cause us to curtail or stop the manufacture of such products until we obtain regulatory compliance.

With respect to commercial supply arrangements, we currently have such an arrangement in place for PIXUVRI, but we do not presently have one in place for pacritinib (or for our other product candidates). In particular, as we have continued to advance the development of pacritinib and position such product for potential commercialization, procuring a qualified commercial supplier for pacritinib has become an important objective.

Any failure or delay in the manufacturing and testing of a product or product candidate in compliance with applicable regulations, or in obtaining and maintaining qualified vendors (including qualified commercial suppliers) to provide the requisite services when needed, could delay the clinical development and commercialization of the applicable product or product candidate and harm our business.

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Our financial condition may be harmed if third parties default in the performance of contractual obligations.

Our business is dependent on the performance by third parties of their responsibilities under contractual relationships. In September 2012, our wholly-owned subsidiary CTI Life Sciences Limited, or CTILS, entered into a Logistics Agreement with Movianto Nederland BV, or Movianto, pursuant to which Movianto agreed to provide certain warehousing, transportation, distribution, order processing and cash collection services and all related activities to CTILS and its affiliates for PIXUVRI in certain agreed territories in Europe. Movianto provides a variety of services related to our sales of PIXUVRI, including receipt, unloading and checking, warehousing and inventory control; customer order management; distribution and transportation; lot number and expiry date control; returned goods processing; return and recall; product quality assurance; and reporting, credit management and debt collection. If Movianto, or other third parties we may enter into contracts with default on the performance of their contractual obligations, we could suffer significant financial losses and operational problems, which could in turn adversely affect our financial performance, cash flows or operating results and may jeopardize our ability to maintain our operations.

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

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

- In Europe, PIXUVRI faces competition from existing treatments for adults with multiply relapsed or refractory aggressive B-cell NHL. For example, patients are currently being treated with bendamustine, oxaliplatin and gemcitabine, although these particular agents do not have regulatory approval in Europe for the foregoing indication. If we were to pursue bringing PIXUVRI to market in the U.S. (which is not currently part of our near-term plan), PIXUVRI would face similar competition. In addition, PIXUVRI may face competition in the E.U. (and, if applicable in the future, the U.S.) if new anti-cancer drugs with reduced toxicity and/or increased efficacy are developed and marketed in the E.U. and/or the U.S.

- If we are successful in bringing pacritinib to market, pacritinib will face competition from ruxolitinib (Jakafi®) and new drugs targeting similar diseases that may be developed and marketed.

- If we are successful in bringing Opaxio to market, we will face direct competition from oncology-focused multinational corporations. Opaxio will compete with other taxanes. Many oncology-focused multinational corporations currently market or are developing taxanes, epothilones, and other cytotoxic agents, which inhibit cancer cells by a mechanism similar to taxanes, or similar products. Such corporations include, among others, Bristol-Myers Squibb Co., which market paclitaxel and generic forms of paclitaxel; Sanofi-Aventis U.S. LLC, which markets docetaxel; Genentech, Inc., Hoffmann-La Roche Inc. and Astellas Pharma US, Inc., which market Tarceva ; Genentech, Inc. and Hoffmann-La Roche Inc., which market Avastin ; Eli Lilly & Company, which markets Alimta®; and Celgene Corporation, which markets Abraxane . In addition, other companies such as Telik, Inc. are also developing products, which could compete with Opaxio.

- If we are successful in bringing tosedostat to market, tosedostat will face competition from currently marketed products, such as cytarabine, Dacogen®, Vidaza®, Clolar®, Revlimid®, Thalomid® and new anti-cancer drugs that may be developed and marketed.

Many of our competitors, particularly the multinational pharmaceutical companies, either alone or together with their collaborators, have substantially greater financial and technical resources and substantially larger development and marketing teams than us, as well as significantly greater experience than we do in developing, manufacturing and marketing products. As a result, products of our competitors might come to market sooner or

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might prove to be more effective, less expensive, have fewer side effects or be easier to administer than ours. In any such case, sales of our current or future products would likely suffer and we might never recoup the significant investments we are making to develop these product candidates.

The pharmaceutical business is subject to increasing government price controls and other restrictions on pricing, reimbursement, and access to drugs, which could affect our future revenues and profitability if new restrictive legislation is adopted.

Legislation and regulations affecting the pricin