CTI BIOPHARMA CORP
Form 10-K
March 02, 2017

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, 2016
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
CTI BIOPHARMA CORP.
(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 ý

As of June 30, 2016, the aggregate market value of the registrant's common equity held by non-affiliates was $65,150,355. 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 23, 2017 was 28,225,792.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2017 annual meeting of shareholders, or the 2017 Proxy Statement, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The 2017 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.

CTI BIOPHARMA CORP.
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Forward Looking Statements

This Annual Report on Form 10-K and the documents we incorporate by reference herein or therein may contain "forward-looking statements" within the meaning of the United States, or the U.S., federal securities laws. All statements other than statements of historical fact are forward-looking statements, including, without limitation:

- any statements regarding future operations, plans, expectations, intentions, regulatory filings or approvals;
- any statements regarding the performance, or likely performance, outcomes or economic benefit of any licensing collaboration or other arrangement;
- 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 and expected sales of PIXUVRI;
- any statements of the plans and objectives of management for future operations or programs;
- any statements concerning proposed new products;
- any statements regarding the safety and efficacy or future availability of any of our compounds;
- any statements regarding our ability to interpret clinical trial data and results or expectations with respect to the potential therapeutic utility of pacritinib and the prevalence of myelofibrosis in the U.S.;
- any statements on plans regarding proposed or potential clinical trials or new drug filing strategies, timelines or submissions, including expectations with respect to the timing and planned enrollment of PAC203;
- any significant disruptions in our information technology systems;
- any statements regarding compliance with the listing standards of The NASDAQ Stock Market and the Mercato Telemarico Azionario, or the MTA, in Italy;
- any statements regarding potential future partnerships, licensing arrangements, mergers, acquisitions or other transactions;
- any statements regarding future economic conditions or performance; and
- any statements of assumption underlying any of the foregoing.

In some cases, forward-looking statements can be identified by terms such as "anticipates," "believes," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should" or "will" or the negative thereof thereof and similar expressions. Such statements are based on management's current expectations and are subject to risks and uncertainties, which may cause actual results to differ materially from those set forth in the forward-looking statements. In particular, this Annual Report on Form 10-K addresses top-line results regarding data from PERSIST-2, our Phase 3 trial of pacritinib for the treatment of patients with myelofibrosis whose platelet counts are less than or equal to 100,000 per microliter. Meaningful interpretation of PERSIST-2 may not be possible because the pre-specified minimum evaluable patient goal was not met. The statements are based on assumptions about many important factors and information currently available to us to the extent we have thus far had an opportunity to fully and carefully evaluate such information in light of all surrounding facts, circumstances, recommendations and analyses. There can be no assurance that such expectations or any of the forward-looking statements will prove to be correct, and actual results could differ materially from those projected or assumed in the forward-looking statements. We urge you to carefully review the disclosures we make concerning risks and other factors that may affect our business and operating results, including those made 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 and any risk factors contained in subsequent Quarterly Reports on Form 10-Q that we file with the U.S. Securities and Exchange Commission, or the SEC.

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.

In this Annual Report on Form 10-K, all references to “we,” “us,” “our,” the “Company” and “CTI” mean CTI BioPharma Co and our subsidiaries, except where it is otherwise made clear.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the acquisition, development and commercialization of novel targeted therapies covering a spectrum of blood-related cancers that offer a unique benefit to patients and health care providers. 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. In particular, we are primarily focused on commercializing PIXUVRI in select countries in the European Union, or the E.U., for multiply relapsed or refractory aggressive B-cell non-Hodgkin lymphoma, or NHL, and evaluating pacritinib for the treatment of adult patients with myelofibrosis.

PIXUVRI

PIXUVRI is a novel aza-anthracenedione with unique structural and physiochemical properties. In May 2012, the European Commission granted conditional marketing authorization in the E.U. for PIXUVRI as a monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive B-cell NHL. 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. As a part of the conditional marketing authorization, we are required to conduct a post-authorization trial, which we refer to as PIX306, comparing PIXUVRI and rituximab with gemcitabine and rituximab in the setting of aggressive B-cell NHL. Although we do not have and are not currently pursuing regulatory approval of PIXUVRI in the United States, or the U.S., we may reevaluate a possible submission strategy in the U.S. based on the data generated from the PIX306 study. Pursuant to our conditional marketing authorization in the E.U., and an extension granted in September 2016 we are required to submit the requisite clinical study report for PIX306 by December 2018.

In September 2014, we entered into an exclusive license and collaboration agreement, or the Servier Agreement, with Les Laboratoires Servier and Institut de Recherches Internationales Servier, or collectively, Servier, with respect to the development and commercialization of PIXUVRI. Under the Servier Agreement, we retain full commercialization rights to PIXUVRI in Austria, Denmark, Finland, Germany, Israel, Norway, Sweden, Turkey, the United Kingdom, or the U.K., and the U.S., or collectively, the CTI Territory, while Servier has exclusive rights to commercialize PIXUVRI in all other countries. In February 2015, we received a €1.5 million milestone payment from Servier relating to the attainment of reimbursement approval for PIXUVRI in Spain. In January 2017, we received a €7.5 million milestone payment from Servier following the achievement of a milestone associated with patient enrollment in the Phase 3 PIX306 clinical trial of PIXUVRI.

For additional information on our collaboration with Servier, please see the discussion in “License Agreements and Additional Milestone Activities - Servier” below.

Pacritinib

Our lead development candidate, pacritinib, is an investigational oral kinase inhibitor with specificity for JAK2, FLT3, IRAK1 and CSF1R. 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. In addition to myelofibrosis, the kinase profile of pacritinib suggests its potential therapeutic utility in conditions such as acute myeloid leukemia, or AML, myelodysplastic syndrome, or MDS, chronic myelomonocytic leukemia, or CMML, and chronic lymphocytic leukemia, or CLL, due to its inhibition of c-fms, IRAK1, JAK2 and FLT3. We believe pacritinib has the potential to be delivered as a single agent or in combination therapy regimens.

Pacritinib was evaluated in two Phase 3 clinical trials, known as the PERSIST program, for patients with myelofibrosis, with one trial in a broad set of patients without limitations on platelet counts, the PERSIST-1 trial; and the other in patients with low platelet counts, the PERSIST-2 trial. In August 2014, pacritinib was granted Fast Track designation by the FDA for the treatment of intermediate and high risk myelofibrosis including, but not limited to, patients with disease-related thrombocytopenia (low platelet counts); patients experiencing treatment-emergent thrombocytopenia on other JAK2

inhibitor therapy; or patients who are intolerant of, or whose symptoms are not well controlled (sub-optimally managed) on other JAK2 therapy.

In May 2015, we announced the final results from PERSIST-1, our Phase 3 trial evaluating the efficacy and safety of pacritinib compared to BAT (Best Available Therapy), excluding JAK2 inhibitors, which included a broad range of currently utilized treatments – in 327 patients with myelofibrosis, regardless of the patients' platelet counts. The study included patients with severe or life-threatening thrombocytopenia. Patients were randomized to receive 400 mg pacritinib once daily or BAT, excluding JAK2 inhibitors. The trial met its primary endpoint of spleen volume reduction (SVR) (35 percent or greater from baseline to Week 24 by magnetic resonance imaging (MRI) or computerized tomography (CT)).

In February 2016, clinical studies under the investigational new drug (IND) for pacritinib were subject to a full clinical hold issued by the FDA. A full clinical hold is a suspension of the clinical work requested under the IND application. Under the full clinical hold, all patients currently on pacritinib were required to discontinue pacritinib immediately and no patients could be enrolled or start pacritinib as initial or crossover treatment. In its written notification, the FDA cited the reasons for the full clinical hold were that it noted interim overall survival results from the PERSIST-2 Phase 3 trial showing a detrimental effect on survival consistent with the results from PERSIST-1.
In February 2016, prior to the clinical hold we completed patient enrollment in the PERSIST-2 Phase 3 clinical trial. Under the full clinical hold, all patients participating in the PERSIST-2 clinical trial discontinued pacritinib treatment.

In August 2016, we announced the top-line results from PERSIST-2, our Phase 3 trial of pacritinib for the treatment of patients with myelofibrosis whose platelet counts are less than or equal to 100,000 per microliter. Three hundred eleven (311) patients were enrolled in the study, which formed the basis for the safety analysis. Two hundred twenty-one (221) patients had a chance to reach Week 24 (the primary analysis time point) at the time the clinical hold was imposed and constituted the intent-to-treat analysis population utilized for the evaluation of efficacy. Results demonstrated that the PERSIST-2 trial met one of the co-primary endpoints showing a statistically significant response rate in spleen volume reduction in patients with myelofibrosis treated with pacritinib compared to BAT, including the approved JAK2 inhibitor ruxolitinib. The co-primary endpoint of reduction of Total Symptom Score (TSS) was not achieved but trended toward improvement in TSS. Irrespective of prior ruxolitinib treatment, pacritinib therapy resulted in a statistically significant higher proportion of patients with SVR than patients on BAT. There was no significant difference in overall survival (OS) across treatment arms, censored at the time of clinical hold. The most common treatment-emergent adverse events (AEs), occurring in 20 percent or more of patients treated with pacritinib within 24 weeks, of any grade, were gastrointestinal (generally manageable diarrhea, nausea and vomiting) and hematologic (anemia and thrombocytopenia) and were generally less frequent for twice-daily (BID) versus once-daily (QD) administration. Details of the trial were presented in a late-breaking oral session at the American Society of Hematology Annual Meeting in December 2016.
In January 2017, the FDA removed the full clinical hold following review of our complete response submission which included, among other items, final Clinical Study Reports for both PERSIST-1 and 2 trials and a dose-exploration clinical trial protocol that the FDA requested. At that time, we announced that we intend to conduct a new trial, PAC203, that plans to enroll up to approximately 105 patients with primary myelofibrosis who have failed prior ruxolitinib therapy to evaluate the dose response relationship for safety and efficacy (spleen volume reduction at 12 and 24 weeks) of three dose regimens: 100 mg QD, 100 mg BID and 200 mg BID. The 200 mg BID dose regimen was used in PERSIST-2. The Company expects to start the trial in the second quarter of 2017.

Other Pipeline Candidates

Our earlier stage product candidate, tosedostat, is a novel oral, once-daily aminopeptidase inhibitor that has demonstrated significant responses in patients with AML. It is currently being evaluated in several Phase 2 cooperative group-sponsored trials and investigator-sponsored trials, or ISTs. These trials are evaluating tosedostat in

combination with hypomethylating agents in AML and MDS, which are cancers of the blood and bone marrow. We anticipate data from these signal-finding trials may be used to determine an appropriate design for a Phase 3 trial.

Our Strategy

Our objective 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 to achieve these objectives are to:

- Commercialize PIXUVRI. Together with Servier, we intend to continue our efforts to build a successful PIXUVRI franchise in Europe as well as other markets. We and our partner 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 available. A successful outcome from the post-authorization trial, PIX306, will enable us to potentially obtain full marketing authorization from the European Commission and expand the market potential for PIXUVRI.

- Develop Pacritinib in Myelofibrosis and Additional Indications. We intend to develop and commercialize pacritinib for adult patients with myelofibrosis and potentially additional indications.

- Continue to Develop Tosedostat for AML and MDS. We intend to continue to develop our earlier stage candidate tosedostat for the treatment of AML and MDS currently through cooperative group sponsored trials and ISTs. Sponsoring such trials provides us with a more economical approach for further developing our investigational products.

- Evaluate Strategic Product Collaborations to Accelerate Development and Commercialization. Where we believe it may be beneficial, we intend to evaluate 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 Development Portfolio

The following table summarizes our current product and development portfolio as of March 2, 2017:

	Indications/Intended Use	Status
PIXUVRI (pixantrone)	Multiply relapsed aggressive B-cell NHL	Marketed in E.U.; Conditional Marketing Authorization
	Aggressive NHL, 2nd line >1 relapse, combination with rituximab (PIX306) post-approval study	Phase 3: Enrollment ongoing
Pacritinib	Myelofibrosis, PERSIST-1, All platelet levels	Phase 3: Trial completed; Final results presented at medical meeting
	Myelofibrosis, PERSIST-2, Platelet counts ≤100,000/μL	Phase 3: Trial completed; Final results presented at medical meeting
	Other hematological and solid tumor indications	Phase 2: Multiple studies ongoing(1)
Tosedostat	AML/MDS	Phase 2: Multiple studies ongoing(1)

(1) We support the development of these investigational agents through cooperative group sponsored trials and ISTs.

Oncology Market Overview and Opportunity

According to the American Cancer Society, or ACS, cancer is the second leading cause of death in the U.S., resulting in close to 595,690 deaths annually, or more than 1,630 people per day. Approximately 1.7 million new cases of cancer were expected to be diagnosed in 2016 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.

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We believe our expertise in blood-related cancers, together with our ability to identify unique therapies that address unmet medical needs that are potentially less toxic and more effective at treating and curing patients, fills a significant unmet medical need for cancer patients.

Commercialized Product

PIXUVRI

Overview
PIXUVRI is a novel aza-anthracenedione with unique structural and physiochemical properties. In May 2012, the European Commission granted conditional marketing authorization in the E.U. for PIXUVRI as a monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive B-cell NHL. 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. As a part of the conditional marketing authorization, we are required to conduct a post-authorization trial, which we refer to as PIX306, comparing PIXUVRI and rituximab with gemcitabine and rituximab in the setting of aggressive B-cell NHL. Although we do not have and are not currently pursuing regulatory approval of PIXUVRI in the U.S., we may reevaluate a possible submission strategy in the U.S. based on the data generated from the PIX306 study. Pursuant to our conditional marketing authorization in the E.U., and an extension granted in September 2016 we are required to submit the requisite clinical study report for PIX306 by December 2018.

PIXUVRI for the Treatment of NHL

We are specifically developing and commercializing PIXUVRI for the treatment of aggressive NHL. NHL is caused by the abnormal proliferation of lymphocytes, which are cells key to the functioning of the immune system. NHL usually originates in lymph nodes and spreads through the lymphatic system. The ACS estimated that there would be 72,580 people diagnosed with NHL in the U.S. and approximately 20,150 people would die from this disease in 2016. The World Health Organization's International Agency for Research on Cancer's 2012 GLOBOCAN database estimates that, in the E.U., approximately 79,312 people will be diagnosed with NHL and 30,730 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.

Aggressive B-cell NHL is the most common subtype, accounting for about 55 percent of NHL cases. After initial therapy for aggressive NHL with anthracycline-based combination therapy, one-third of patients typically develop progressive disease. 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 only. PIXUVRI is the first treatment approved in the E.U. for patients with multiply relapsed or refractory aggressive B-cell NHL.

Commercialization of PIXUVRI in the E.U.

In September 2012, we initiated E.U. commercialization of PIXUVRI and in September 2014 we entered into a collaboration arrangement with Servier. Under the Servier Agreement, we retain full commercialization rights to PIXUVRI in Austria, Denmark, Finland, Germany, Israel, Norway, Sweden, Turkey, the United Kingdom, or the U.K., and the U.S., or collectively, the CTI Territory, while Servier has exclusive rights to commercialize PIXUVRI in all other countries. For additional information on our collaboration with Servier, please see the discussion in "License Agreements and Additional Milestone Activities - Servier."

As discussed in Part I, Item 1, “Business-Manufacturing, Distribution and Associated Operations,” we utilize third parties for the manufacture, storage and distribution of PIXUVRI, as well as for other associated supply chain operations. Our strategy of utilizing third parties in such manner allows us to direct our resources to the development and commercialization of compounds rather than to the establishment and maintenance of facilities for such operational activities.

Development Candidates

Pacritinib

Development in Myelofibrosis

Our lead development candidate, pacritinib, is an investigational oral kinase inhibitor with specificity for JAK2, FLT3, IRAK1 and CSF1R. 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. In addition to myelofibrosis, the kinase profile of pacritinib suggests its potential therapeutic utility in conditions such as acute myeloid leukemia, or AML, myelodysplastic syndrome, or MDS, chronic myelomonocytic leukemia, or CMML, and chronic lymphocytic leukemia, or CLL, due to its inhibition of c-fms, IRAK1, JAK2 and FLT3. We believe pacritinib has the potential to be delivered as a single agent or in combination therapy regimens.

In August 2014, pacritinib was granted Fast Track designation by the FDA for the treatment of intermediate and high risk myelofibrosis, including, but not limited, to patients with disease-related thrombocytopenia, patients experiencing treatment-emergent thrombocytopenia on other JAK2 therapy or patients who are intolerant of, or whose symptoms are sub-optimally managed on, other JAK2 therapy. The FDA's Fast Track process is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.

We are pursuing a comprehensive approach to advancing pacritinib for adult patients with myelofibrosis and have completed two Phase 3 clinical trials: one in a broad set of patients without limitations on blood platelet counts, the PERSIST-1 trial; and the other in patients with low platelet counts, the PERSIST-2 trial. Myelofibrosis is a rare blood cancer associated with significantly reduced quality of life and shortened survival. As the disease progresses, the body slows production of important blood cells and within one year of diagnosis, the incidence of disease-related thrombocytopenia (very low blood platelet counts), severe anemia and red blood cell transfusion requirements increase significantly. Among other complications, most patients with myelofibrosis present with enlarged spleens (splenomegaly), as well as many other potentially devastating physical symptoms such as abdominal discomfort, bone pain, feeling full after eating little, severe itching, night sweats and extreme fatigue. Currently patients with very low blood platelets (<50,000/μL) or those ineligible to receive, intolerant of or have insufficient response to the approved JAK1/JAK2 inhibitor have no effective treatment options. We believe 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 the approved JAK1/JAK2 inhibitor.

PERSIST-1 was a randomized (2:1), open-label, multi-center Phase 3 trial comparing the efficacy and safety of pacritinib with that of best available therapy other than JAK inhibitors, in 327 patients with myelofibrosis, without exclusion for low platelet counts. The primary endpoint for PERSIST-1 was the proportion of patients achieving a 35 percent or greater reduction in spleen volume from baseline to Week 24 as measured by MRI or CT, when compared with physician-specified BAT, excluding treatment with JAK2 inhibitors. The secondary endpoint was the percentage of patients achieving a 50 percent or greater reduction in Total Symptom Score, or TSS, from baseline to week 24 as measured by tracking specific symptoms on a form, or Patient Reported Outcome, or PRO, instrument. At study entry, 46 percent of patients were thrombocytopenic; 32 percent of patients had platelet counts less than 100,000 per microliter (<100,000/μL); and 16 percent of patients had platelet counts less than 50,000 per microliter (<50,000/μL); normal platelet counts range from 150,000 to 450,000 per microliter. At the time of initiation of the trial, PERSIST-1 utilized the Myeloproliferative Neoplasm Symptom Assessment Form, or MPN-SAF TSS, the PRO instrument developed by Mayo Clinic, to measure TSS reduction. We collaborated with Mayo Clinic and the FDA and developed a modified instrument to be used as the endpoint for pacritinib clinical development. As a result, we amended 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. In connection with this amendment, we increased patient enrollment in the PERSIST-1 study from 270 to 327 patients.

In May 2015, data from PERSIST-1 showed that compared to BAT (exclusive of a JAK inhibitor) pacritinib therapy resulted in a significantly higher proportion of patients with spleen volume reduction and control of disease-related symptoms meeting the primary endpoint of the trial. Results were presented at a late-breaking oral session at the 51st Annual Meeting of the American Society of Clinical Oncology. Additionally, in June 2015, results from PERSIST-1 PRO and other quality of life measures presented at a late-breaking oral session at the 20th Congress of the European Hematology Association showed significant improvements in symptom score with pacritinib therapy compared to BAT (exclusive of a JAK inhibitor) across the symptoms reported in the presentation.

The following table shows the proportion of patients randomized to pacritinib or best available treatment, or BAT, who achieved a ≥35% reduction in spleen volume from baseline at Week 24 or up to Week 24 in the intent-to-treat, or ITT,

population or evaluable patient population. The greatest difference in treatment arms was observed in evaluable patients with the lowest platelet counts (<50,000/μL platelets) (33.3 percent with pacritinib vs 0 percent with BAT) (p=0.037).

Spleen Volume Reduction of ≥35% at Week 24 by Platelet Levels

	Pacritinib	BAT	p-value
All Platelet Levels			
ITT*	19.1% (n=220)	4.7% (n=107)	0.0003
Evaluable**	25.0% (n=168)	5.9% (n=85)	<0.0001
<100,000/μL platelets			
ITT	16.7% (n=72)	0% (n=34)	0.0086
Evaluable	23.5% (n=51)	0% (n=24)	0.0072
<50,000/μL platelets			
ITT	22.9% (n=35)	0% (n=16)	0.0451
Evaluable	33.3% (n=24)	0% (n=11)	0.0370

* ITT - primary analysis included all patients randomized. Patients who missed MRI or CT scans at baseline or at Week 24 were counted as non-responders.
** Evaluable - analysis included patients who had assessment at both baseline and at Week 24.

Results from PERSIST-1 PRO and other quality of life measures showed significant improvements in symptom score with pacritinib therapy compared to BAT (exclusive of a JAK inhibitor) across the symptoms reported in the presentation. Patients treated with pacritinib experienced greater improvement in their disease-related symptoms (ITT patient population: 24.5 percent of pacritinib-treated patients vs 6.5 percent of BAT-treated patients, p<0.0001; evaluable patient population: 40.9 percent of pacritinib-treated patients vs 9.9 percent of BAT-treated patients, p<0.0001).

Additionally, 25 percent of patients treated with pacritinib who were severely anemic and transfusion dependent - requiring at least six units of blood in the 90 days prior to study entry - became transfusion independent, compared to zero patients treated with BAT (p<0.05). Among patients with the lowest baseline platelets (<50,000/μL) who received treatment with pacritinib, a significant increase in platelet counts was observed over time compared to BAT (p=0.003) - with a 35 percent increase in platelet counts from baseline to Week 24.

The most common adverse events, occurring in 10 percent or more of patients treated with pacritinib within 24 weeks, of any grade, were: mild to moderate diarrhea, nausea, anemia, thrombocytopenia, and vomiting. Of the patients treated with pacritinib, 3 discontinued therapy and 13 patients required dose interruption (average one week) for diarrhea. Patients received a daily full dose of pacritinib over the duration of treatment. Gastrointestinal symptoms typically lasted for approximately one week and few patients discontinued treatment due to side effects. There were no Grade 4 gastrointestinal events reported.

In December 2015, primarily based on the results of the PERSIST-1 trial, we submitted a New Drug Application, or NDA, to the FDA, for pacritinib requesting U.S. marketing approval of pacritinib for the treatment of patients with intermediate and high-risk myelofibrosis with low platelet counts of less than 50,000 per microliter (<50,000/μL) for whom there are no approved therapies.

The PERSIST-2 trial was a randomized (2:1), open-label, multi-center registration-directed Phase 3 trial evaluating pacritinib compared to best available therapy, or BAT, including the approved JAK inhibitor dosed according to product label, for patients with myelofibrosis whose platelet counts are less than or equal to 100,000 per microliter (≤100,000/μL). Patients were randomized to receive 200 mg pacritinib twice daily, 400 mg pacritinib once daily or

BAT. In October 2013, we reached an agreement with the FDA on a Special Protocol Assessment, or SPA, for the PERSIST-2 trial regarding the planned design, endpoints and statistical analysis approach of the trial. The SPA is a written agreement between us and the FDA regarding the design, endpoints and planned statistical analysis approach of the trial to be used in support of a NDA submission. Under the SPA, the agreed upon co-primary endpoints are the percentage of patients achieving a 35% or greater reduction in spleen volume measured by MRI or CT scan from baseline to Week 24 of treatment and the percentage of patients achieving a TSS reduction of 50% or greater using eight key symptoms as measured by the modified MPN-SAF TSS 2.0 diary from baseline to Week 24. The design of PERSIST-1 and PERSIST-2 allowed for patients on the BAT arm to crossover and receive treatment with pacritinib if their disease progresses or after they achieve the 24-week measurement endpoint. Although crossover design

of clinical trials may confound evaluation of survival, such designs are frequently used in cancer studies, and the FDA has approved multiple oncology drugs that utilized crossover design in Phase 3 trials.
In February 2015, we received a recommendation from the independent Data Monitoring Committee, or IDMC, in place at the time to terminate the PERSIST-1 trial and hold enrollment of new patients in the PERSIST-2 trial. The IDMC's recommendation was based on non-statistically significant safety concerns, including mortality, in patients on pacritinib, particularly those who crossover after 24 weeks, which crossover potentially confounds evaluation of survival. The IDMC agreed that the recommendation would be only preliminary until we were unblinded to and could review the primary and secondary endpoint data as well as safety results from the PERSIST-1 trial. The PERSIST IDMC charter explicitly reserved the final decision regarding whether to implement the recommendations with us. The IDMC recommendation was reviewed with the PERSIST Steering Committee, comprised of external experts and the study's principal investigators. The PERSIST Steering Committee disagreed with the IDMC's recommendation and expressed the view that the studies should continue as planned. We also asked an independent clinician and a statistician experienced in oversight of clinical trial safety to evaluate the safety profile of pacritinib in the PERSIST-1 trial. Neither was told of the recommendation reached by either the IDMC or the Steering Committee. Both experts agreed with the Steering Committee that the studies could continue. Given the opinions of the external experts and the Steering Committee, the firm that assembled the IDMC and assisted it in its duties hired a second external independent statistician to review the IDMC's analyses and recommendation. The second statistician also disagreed with the IDMC recommendation and concurred that the studies need not be terminated or enrollment held. The IDMC made its recommendation final in June 2015, at which time we provided to the FDA the information reviewed by the IDMC, as well as the IDMC's meeting minutes, the written opinion of the Steering Committee co-chairs, the external experts, and the second independent statistician. In July 2015, we requested a meeting with the FDA to confirm whether the FDA agreed with our decision to continue the studies. The FDA assigned the request to a type C meeting and responded in writing to us. The FDA did not mandate any modifications to the studies or place pacritinib on clinical hold at that time, but indicated that it had not yet reviewed the data and noted the difficulty in attempting to draw meaningful conclusions from non-significant results, and that the crossover designs may confound the analysis of survival. We determined that no modifications to the ongoing trials were required. Because we had concerns about the original IDMC's impartiality, we decided to discharge it, and through an independent firm specializing in IDMCs, retained a new IDMC. The newly constituted IDMC met on several occasions, including following the FDA decision to place the pacritinib program on full clinical hold. Its recommendation was to continue PERSIST-2 as planned.

On February 8, 2016, the FDA notified us that a full clinical hold has been placed on pacritinib clinical studies. A full clinical hold is a suspension of the clinical work requested under the investigational new drug, or an IND, application. Under the full clinical hold, all patients currently on pacritinib were required to discontinue pacritinib immediately and no patients could be enrolled or start pacritinib as initial or crossover treatment. In its written notification, the FDA cited the reasons for the full clinical hold were that it noted interim overall survival results from the PERSIST-2 Phase 3 trial showing a detrimental effect on survival consistent with the results from PERSIST-1. The deaths in PERSIST-2 in pacritinib-treated patients include intracranial hemorrhage, cardiac failure and cardiac arrest. In connection with the full clinical hold, the FDA has recommended that we conduct Phase 1 dose exploration studies of pacritinib in patients with myelofibrosis, submit final clinical study reports, or CSRs, and datasets for PERSIST-1 and PERSIST-2, provide certain notifications, revise relevant statements in the related Investigator's Brochure and informed consent documents and make certain modifications to protocols. In addition, the FDA recommended that we request a meeting prior to submitting a response to full clinical hold. As a result of the full clinical hold of pacritinib, the SPA agreement is no longer binding for PERSIST-2, and we have withdrawn the NDA.
In February 2016, prior to the clinical hold we completed patient enrollment in the PERSIST-2 Phase 3 clinical trial. Under the full clinical hold, all patients participating in the PERSIST-2 clinical trial discontinued pacritinib treatment.

In August 2016, we announced the top-line results from PERSIST-2, and the detailed results were presented in a late-breaking oral session at the American Society of Hematology Annual Meeting in December 2016. In the PERSIST-2 trial 311 patients were randomized to receive 200 mg pacritinib BID, 400 mg pacritinib QD or BAT. Two

hundred twenty-one (221) patients (74 pacritinib BID; 75 pacritinib QD; 72 BAT) were enrolled at least 24 weeks prior to the full clinical hold and were potentially evaluable for the Week 24 efficacy endpoint (ITT efficacy population). In the ITT efficacy population at study entry, 46 percent (101/221) of patients had platelet counts less than 50,000 per microliter (<50,000/μL), and 59 percent (130/221) were anemic (hemoglobin <10 g/dL). Normal platelet counts range from 150,000 to 450,000 per microliter. The percentage of patients in the ITT efficacy population who received prior ruxolitinib was as follows: 41 percent (31/75) pacritinib QD; 42 percent (31/74) pacritinib BID; and 46 percent (33/72) BAT. Safety analyses were based on all patients exposed to study treatment of any duration.

The co-primary endpoints of the trial were the proportion of patients achieving a 35 percent or greater reduction in spleen volume from baseline to Week 24 as measured by MRI or CT scan and the proportion of patients achieving a TSS reduction of 50 percent or greater using the modified Myeloproliferative Neoplasm Symptom Assessment (MPN-SAF TSS 2.0) diary from baseline to Week 24. The primary objective of the study was to compare pooled pacritinib arms versus BAT and the secondary objectives were to compare pacritinib BID and QD arms individually to BAT. Study was designed to evaluate the study objectives with sample size of 300. At the time of clinical hold, study enrollment was completed with 311 patients randomized, but only 221 patients had the potential to be evaluated for efficacy endpoints at Week 24.

The PERSIST-2 trial met one of the co-primary endpoints showing a statistically significant response rate in SVR in patients with myelofibrosis treated with pacritinib combining the once- and twice-daily arms compared to BAT. Although the PERSIST-2 trial did not meet the other co-primary endpoint of greater than 50 percent reduction in TSS, the results approached marginal significance compared to BAT. Although secondary objectives could not be evaluated formally due to the study not achieving one of the primary objectives, when the two pacritinib dosing arms were evaluated separately versus BAT, pacritinib given twice daily showed a higher percent of SVR and TSS responses compared to BAT; whereas, pacritinib given once daily showed only a higher percent SVR responses compared to BAT.

Spleen Volume Reduction of ≥35%; Total Symptom Score Reduction of ≥50% at Week 24

	Co-Primary Pacritinib BID + QD (n=149)	Secondary Pacritinib BID (n=74)	Secondary Pacritinib QD (n=75)	BAT (n=72)
Percent of Patients with ≥35% SVR from baseline to Week 24	18% (n=27;p=0.001)	22% (n=16;p=0.001)	15% (n=11;p=0.017)	3% (n=2)
Percent of Patients with ≥50% reduction in TSS from baseline to Week 24	25% (n=37;p=0.079)	32% (n=24;p=0.011)	17% (n=13;p=0.652)	14% (n=10)

A total of 45 percent of the BAT patients randomized received ruxolitinib at some point on the study.

There was no significant difference in overall survival (OS) across treatment arms, censored at the time of clinical hold. Hazard ratios (95% confidence intervals (CI)) were 0.68 (0.30-1.53) for pacritinib BID versus BAT and 1.18 (0.57-2.44) for pacritinib QD versus BAT. Overall mortality rates at that time were comparable between arms: 9 percent BID versus 14 percent QD and 14 percent BAT.

The most common treatment-emergent AEs, occurring in 20 percent or more of patients treated with pacritinib within 24 weeks, of any grade, were gastrointestinal (generally manageable diarrhea, nausea and vomiting) and hematologic (anemia and thrombocytopenia) and were generally less frequent for BID versus QD administration. The most common serious treatment-emergent AEs (incidence of ≥5 percent reported in any treatment arm irrespective of grade) were anemia, thrombocytopenia, pneumonia and acute renal failure none of which exceeded 8 percent individually in any arm.

In January 2017, the FDA removed the full clinical hold following review of our complete response submission which included, among other items, final Clinical Study Reports for both PERSIST-1 and 2 trials and a dose-exploration clinical trial protocol that the FDA requested. At that time, we announced that we intend to conduct a new trial, PAC203, that plans to enroll up to approximately 105 patients with primary myelofibrosis who have failed prior ruxolitinib therapy to evaluate the dose response relationship for safety and efficacy (spleen volume reduction at 12

and 24 weeks) of three dose regimens: 100 mg once-daily, 100 mg twice-daily (BID) and 200 mg BID. The 200 mg BID dose regimen was used in PERSIST-2. We expect to start the trial in the second quarter of 2017.

Marketing Authorization Application

The Marketing Authorization Application (MAA) for pacritinib was submitted to the European Medicines Agency (EMA) in February 2016 with an indication statement based on the PERSIST-1 trial data. In its initial assessment report, the Committee for Medicinal Products for Human Use (CHMP) determined that the current application is not approvable because of major objections in the areas of efficacy, safety (hematological and cardiovascular toxicity) and the overall risk-benefit

profile of pacritinib. Subsequent to the filing of the MAA, data from the second phase 3 trial of pacritinib, PERSIST-2, were reported. These data suggest that pacritinib may show clinical benefit in patients who have failed or are intolerant to ruxolitinib therapy, a population for which there is no approved therapy.

Following discussions with the EMA about how PERSIST-2 data might address the major objections and how to integrate the data into the current application, we have decided to withdraw the MAA. We are preparing a new MAA that seeks to address the major objections by including data from PERSIST-2. The new application will focus on patients who have failed or are intolerant to ruxolitinib. We plan to submit this new application in the second quarter of 2017.

Development in Other Indications

In December 2014, we announced results of a preclinical analysis of kinase inhibition by pacritinib that demonstrated a unique kinome profile among agents in development for myelofibrosis and suggests potential therapeutic benefit across a spectrum of blood-related cancers. Pacritinib's potent inhibition of FLT3, c-fms, IRAK1 and c-kit highlight its potential therapeutic utility in other indications, such as AML, MDS, CMML and CLL, some of which are currently being evaluated in ISTs.

In October 2016, we regained worldwide rights for the development and commercialization of pacritinib following termination of the Pacritinib License Agreement with Baxalta. For additional information relating to the termination of the Pacritinib License Agreement, see "License Agreements and Additional Milestone Activities - Baxalta" below.

Tosedostat

Tosedostat is a first-in-class selective inhibitor of aminopeptidases, which are required by tumor cells to provide amino acids necessary for growth and tumor cell survival. Tosedostat has demonstrated anti-tumor responses in blood-related cancers and solid tumors in Phase 1 and 2 clinical studies. Specifically, study results presented for tosedostat in AML have shown promising complete response, or CR, rates and good tolerability. It is currently being evaluated in several Phase 2 cooperative group-sponsored trials and ISTs. These trials are evaluating tosedostat in combination with hypomethylating agents in AML and MDS, which are cancers of the blood and bone marrow. We anticipate data from these signal-finding trials may be used to determine an appropriate design for a Phase 3 trial.

In June 2014, we announced the initiation of an international cooperative group Phase 2/3 clinical trial of tosedostat in combination with low-dose cytarabine in older patients with AML or high risk MDS. The study is being conducted by the National Cancer Research Institute (NCRI) Haematological Oncology Study Group under the sponsorship of Cardiff University. In this Phase 2/3 study, referred to as AML Less Intensive or LI-1, patients are being randomized to standard treatment, low dose cytarabine, versus other novel investigational treatments, one of which is tosedostat, each in combination with low dose cytarabine. The trial utilizes a "Pick a Winner" trial design. Overall survival is the primary endpoint of this trial.

In November 2015, based on the randomized Phase 2 interim analysis of the LI-1 study, the trial management group determined that tosedostat should proceed to the next stage of the study. The aim of the trial is to identify treatments that can double the 2-year survival of patients in this group. It is anticipated that an additional 110 patients will be required in such phase. A further evaluation will take place before the intended expansion to a 400 patient Phase 3 trial.

In December 2015, results from a separate investigator-sponsored Phase 2 trial of tosedostat in combination with low-dose cytarabine/Ara-C, or LDAC, in elderly patients with either primary AML or AML were presented at the American Society of Hematology Annual Meeting. The Phase 2 multicenter clinical trial was designed to assess

tosedostat (orally once-daily) in combination with intermittent LDAC (twice daily) in 33 elderly patients (median age = 75 years) with either primary AML or secondary AML. This presentation reported on the results of 33 patients (median age was 75) that were enrolled. The study met the primary endpoint with an overall response rate (ORR) of 54.6 percent (n=18/33) in the ITT population. The study achieved a CR rate of 48.5 percent (n=16/33) and the median time for achieving best response was 74 days (range: 22-145 days) with 33 percent still in remission (or experiencing a CR) after a median follow-up of 506 days. Safety analysis show that tosedostat in combination with LDAC was generally well tolerated. The primary adverse events observed were pneumonitis (12 percent), cardiac (6 percent), brain hemorrhage (3 percent), and asthenia (3 percent).

Opaxio

Opaxio™, paclitaxel poliglumex, has been evaluated as a maintenance therapy in ovarian cancer through a cooperative group-sponsored Phase 3 clinical trial by GOG Foundation, Inc. (formerly the Gynecologic Oncology Group and currently a

member of NRG Oncology). The GOG-0212 trial 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 platinum-taxane based therapy.
In July 2016, the GOG Foundation, Inc. reported to us that based on the DMC review of the interim analyses of the GOG-0212 trial, it is unlikely that paclitaxel poliglumex or paclitaxel would demonstrate it is superior to no adjuvant therapy in overall survival, and that the DMC recommended releasing the study results early. Detailed results are expected to be presented at an upcoming scientific meeting.

In February 2017, our exclusive worldwide license for rights to paclitaxel poligumex and certain polymer technology from PG-TXL Company, L.P., or PG-TXL, was terminated as discussed below in Part I, Item 1, “Business - License Agreements and Additional Milestone Activities - PG-TXL”. No further development of paclitaxel poliglumex is planned.
Management and Board of Directors
In February 2017, we announced the appointment of Adam Craig, M.D., Ph.D., as President and Chief Executive Officer (CEO) and member of the Board of Directors effective March 20, 2017. Dr. Craig has over 20 years of experience in hematology, oncology and drug development in both the US and Europe. Dr. Craig worked as an independent consultant providing strategic and operational advice and support to CTI BioPharma and other hematology/oncology biotechnology companies. Prior to consulting, Dr. Craig was Chief Medical Officer (CMO) and Executive Vice President of Development at Sunesis Pharmaceuticals from 2012 to 2016. From 2008 to 2012, Dr. Craig was CMO and Senior Vice President of Chemgenex Pharmaceuticals Ltd. Dr. Craig is a Member of the Royal College of Physicians (UK) and undertook Post-Graduate Training in Pediatrics and Pediatric Oncology. Dr. Craig earned his Bachelor's and Medical degrees from Charing Cross and Westminster Medical School, University of London and holds a Ph.D. in Molecular Oncology from Leeds University in the U.K. and an MBA from the Open Business School, in the United Kingdom. Dr. Craig recently served as a Product Development Reviewer for the Cancer Prevention Research Institute of Texas.
In October 2016, we announced that James A. Bianco, M.D. retired from his position as president and chief executive officer. At the request of the Board of Directors, Richard Love, a director of the Company since 2007, was appointed to serve as interim president and chief executive officer. Mr. Love started two biotechnology companies, Triton Biosciences Inc. and ILEX Oncology Inc., and he served as Chief Executive Officer for Triton Biosciences Inc. from 1983 to 1991 and as Chief Executive Officer for ILEX Oncology from 1994 to 2001. Mr. Love also served in executive positions at not-for-profit organizations including the Cancer Therapy and Research Center (CTRC) and the Translational Genomics Research Institute (TGen).
In January 2017, we announced that Michael A. Metzger was appointed a Director of CTI BioPharma. Mr. Metzger is currently president and chief operating officer of Syndax Pharmaceuticals, Inc., a publicly traded immuno-oncology biopharmaceutical company. Mr. Metzger served as president and chief executive officer of Regado Biosciences, Inc., a former publicly traded biotechnology company, from 2013 to 2015, where he oversaw the company's successful merger with Tobira Therapeutics, Inc. in 2015 and acted as an advisor to Tobira during its subsequent sale to Allergan in 2016. Previously, Mr. Metzger served as executive vice president and chief operating officer at Mersana Therapeutics, a privately held biotechnology company developing novel immunoconjugate therapies for cancer, from 2011 to 2013 and in senior business development positions including leading mergers and acquisitions at Forest Laboratories, Inc. from 2006 to 2011. Mr. Metzger served as vice president corporate development at Onconova Therapeutics, Inc., from 2001 until 2006, and was a managing director at MESA Partners, Inc., a venture capital firm, from 1997 to 2001.

Research and Development Expenses

Research and development is essential to our business. We spent $65.0 million, $76.6 million and $64.6 million in 2016, 2015 and 2014, 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 and tosedostat or to complete the post-approval commitment study of PIXUVRI. Further, third parties are conducting clinical trials for tosedostat and pacritinib. 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, if ever, we will generate material net cash inflows from PIXUVRI or be able to commence commercialization of pacritinib and tosedostat. For additional information relating to our research and development expenses and associated risks, see Part II, Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations - Results of Operations - Years ended December 31, 2016, 2015 and 2014 - Operating costs and expenses - Research and development expenses” and Part I, Item 1A, “Risk Factors”.

License Agreements and Additional Milestone Activities

Servier

In September 2014, we entered into the Servier Agreement pursuant to which we granted Servier an exclusive and sublicensable (subject to certain conditions) royalty-bearing license with respect to the development and commercialization of PIXUVRI for use in pharmaceutical products outside of the CTI Territory (defined below). We retained rights to PIXUVRI in Austria, Denmark, Finland, Germany, Israel, Norway, Sweden, Turkey, the U.K. and the U.S., or collectively, the CTI Territory.

We received an upfront payment in October 2014 of €14.0 million (or $17.8 million using the currency exchange rate as of the date we received the funds in October 2014). In addition, subject to the achievement of certain conditions, the Servier Agreement provides for us to potentially receive milestone payments thereunder in the aggregate amount of up to €89.0 million, which is comprised of the following: up to €49.0 million in potential clinical and regulatory milestone payments (of which €9.5 million is payable upon occurrence of certain enrollment events in connection with the PIX306 study for PIXUVRI); and up to €40.0 million in potential sales-based milestone payments. As of March 2, 2017, of these potential milestone payments, we have received a €1.5 million (or $1.7 million upon conversion from euros as of the date we received the funds) milestone payment relating to the attainment of reimbursement approval for PIXUVRI in Spain and a €7.5 million (or $8.0 million upon conversion from euros as of the date we achieved the milestone in December 2016) milestone payment relating to the occurrence of a certain enrollment event in the PIX306 study. In addition, for a number of years following the first commercial sale of a product containing PIXUVRI in the respective country, regardless of patent expiration or expiration of regulatory exclusivity rights, we are eligible to receive tiered royalty payments ranging from a low-double digit percentage up to a percentage in the mid-twenties based on net sales of PIXUVRI products, subject to certain reductions of up to mid-double digit percentages under certain circumstances.

Unless otherwise agreed by the parties, (i) certain development costs incurred pursuant to a development plan and (ii) certain marketing costs incurred pursuant to a marketing plan will be shared equally by the parties, subject to a maximum dollar obligation of each party.

The Servier Agreement will expire on a country-by-country basis upon the expiration of the royalty terms in the countries outside of the CTI Territory, at which time all licenses granted to Servier would become perpetual and

royalty-free. Each party may terminate the Servier Agreement in the event of an uncured repudiatory breach (as defined under English law) of the other party's obligations. Servier may also terminate the Servier Agreement without cause on a country-by-country basis upon written notice to us within a specified time period or upon written notice within a certain period of days in the event of (i) certain safety or public health issues involving PIXUVRI or (ii) cessation of certain marketing authorizations. In the event of a termination prior to the expiration date, rights granted to Servier will terminate, subject to certain exceptions.

Baxalta

In November 2013, we entered into a Development, Commercialization and License Agreement, dated as of November 14, 2013, between Baxter International Inc., or Baxter, and the Company, for the development and commercialization of pacritinib for use in oncology and potentially additional therapeutic areas, or the Original Pacritinib License Agreement. The

Original Pacritinib License Agreement, the rights and obligations to which Baxter had assigned to Baxalta, which is now part of Shire plc, was amended by the License Amendment, effective June 8, 2015. The Original Pacritinib License Agreement, as amended by the License Amendment, is referred to herein as the “Pacritinib License Agreement”. Under the Pacritinib License Agreement, Baxalta had an exclusive, worldwide (subject to co-promotion rights discussed below), royalty-bearing, non-transferable license (which is sub-licensable under certain circumstances) relating to pacritinib. Licensed products under the Pacritinib License Agreement consisted of products in which pacritinib is an ingredient.

We received an upfront payment of $60.0 million under the Pacritinib License Agreement, which included a $30.0 million investment in our equity. The Pacritinib License Agreement also provided for us to receive potential additional payments of up to $302.0 million upon the successful achievement of certain development and commercialization milestones, comprised of $112.0 million of potential clinical, regulatory and commercial launch milestone payments, and potential additional sales milestone payments of up to $190.0 million. To date, we have received milestone payments of $52.0 million.

In June 2015, we entered into the License Amendment. Pursuant to the License Amendment, two potential milestone payments in the aggregate amount of $32.0 million from Baxalta to us were accelerated from the schedule contemplated by the original Pacritinib License Agreement relating to the PERSIST-2 Milestone and the MAA Milestone. In the first quarter of 2016, we recorded $32.0 million in license and contract revenue upon the attainment of the milestones.

In October 2016, we regained worldwide rights for the development and commercialization of pacritinib following termination of the Pacritinib License Agreement with Baxalta. Pursuant to the termination, Baxalta paid us a one-time cash payment in the amount of approximately $10.3 million as reimbursement for certain expenses incurred or to be incurred. In exchange, we have agreed to provide a one-time payment to Baxalta, upon the first regulatory approval or any pricing and reimbursement approvals of a product containing pacritinib, in the amount of approximately $10.3 million which represents certain amounts paid by Baxalta for the benefit of the pacritinib program manufacturing efforts. We have also agreed not to transfer, license, sublicense or otherwise grant rights with respect to intellectual property of pacritinib unless the transferee/licensee/sublicensee agrees to be bound by the terms of the Asset Return and Termination Agreement with Baxalta. Additional information regarding the Asset Return and Termination Agreement is set forth in Part II, Item 8, "Financial Statements and Supplementary Data, Notes to Consolidated Financial Statements, Note 12. Collaboration, Licensing and Milestone Agreements - Baxalta" of this Annual Report on Form 10-K.

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 sublicensable license 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 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 and FLT3, from 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% 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.

Vernalis

We entered into an amended and restated exclusive license agreement with Vernalis (R&D) Limited, or Vernalis, in October 2014 or the Vernalis License Agreement, for the exclusive worldwide right to use certain patents and other intellectual property rights to develop, market and commercialize tosedostat and certain other compounds. Under the Vernalis License Agreement, we have agreed to make tiered royalty payments of no more than a high single digit percentage of net sales of products containing licensed compounds, with such obligation to continue on a country-by-country basis for the longer of ten years following commercial launch or the expiry of relevant patent claims.

The Vernalis License Agreement will terminate when the royalty obligations expire, although the parties have early termination rights under certain circumstances, including the following: (i) we have the right to terminate, with three months' notice, upon the belief that the continued development of tosedostat or any of the other licensed compounds is not commercially viable; (ii) Vernalis has the right to terminate in the event of our uncured failure to pay sums due; and (iii) either party has the right to terminate in event of the other party's uncured material breach or insolvency.

Gynecologic Oncology Group

We entered into an agreement with the Gynecologic Oncology Group, now part of NRG Oncology, in March 2004, as amended, related to the GOG-0212 trial of Opaxio it is conducting in patients with ovarian cancer. Pursuant to the terms of such agreement, we paid an aggregate of $1.2 million in milestone payments during 2014 based on certain enrollment milestones achieved. We may be required to pay up to an additional $1.0 million upon the attainment of certain other milestones, of which $0.5 million has been recorded in accrued expenses as of December 31, 2016.

PG-TXL

In November 1998, we entered into an agreement with PG-TXL, as amended in February 2006, which granted us an exclusive worldwide license for the rights to Opaxio and to all potential uses of PG-TXL's polymer technology, or the PG-TXL Agreement. 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 were 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 was 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 were required to make royalty payments to PG-TXL based on net sales. Our royalty obligations ranged from low to mid-single digits as a percentage of net sales. In February 2017, we terminated our agreement with PG-TXL and the exclusive worldwide license for rights to Opaxio and certain polymer technology under our agreement with PG-TXL.

Novartis

In January 2014, we entered into a Termination Agreement, or the Novartis Termination Agreement, with Novartis, to reacquire the rights to PIXUVRI previously granted to Novartis under our agreement entered into in September 2006, as amended, or the Original Novartis Agreement. Pursuant to the Novartis Termination Agreement, the Original Novartis Agreement was terminated in its entirety, except for certain customary provisions, including those pertaining to confidentiality and indemnification, which survive termination.

Under the Novartis Termination Agreement, we agreed not to transfer, license, sublicense or otherwise grant rights with respect to intellectual property of PIXUVRI and Opaxio unless the recipient thereof agrees to be bound by the terms of the Novartis 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 PIXUVRI and Opaxio. We are also obligated to pay to Novartis tiered low single-digit percentage royalty payments for the first several hundred million in annual net sales, and 10% royalty payments thereafter based on annual net sales of each of PIXUVRI or Opaxio, subject to reduction in the event generic drugs are introduced and sold by a third party, causing the sale of PIXUVRI to fall by a percentage in the high double-digits. Royalty payments for PIXUVRI are subject to certain minimum floor percentages in the low single digits.

Teva Pharmaceutical Industries Ltd.

In June 2005, we entered into an acquisition agreement with Cephalon, Inc., or Cephalon, pursuant to which we divested the compound, TRISENOX. Cephalon was subsequently acquired by Teva Pharmaceutical Industries Ltd., or Teva. Under this 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. To date, we have received $30.0 million of such potential milestone payments as a result of having achieved certain sales milestones.

Other Agreements

We have several agreements with contract research organizations, third party manufacturers and distributors that have durations of greater than one year for the development and distribution of certain of our compounds.

Information about Customer and Geographic Concentrations

Information about customer and geographic revenue is set forth in Part II, Item 8, "Financial Statements and Supplementary Data, Notes to Consolidated Financial Statements, Note 16. Customer and Geographic Concentrations" of this Annual Report on Form 10-K.

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, 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.

Our PIXUVRI-directed patents currently in force in Europe began to expire in late March 2015 and will continue to expire through a portion of 2023. Some of these European patents are also subject to Supplementary Protection Certificates such that the extended patents will expire from 2020 to 2027. In the United States, our PIXUVRI-directed U.S. patent will expire in 2024. Our PIXUVRI-directed patents outside of Europe and the U.S. began to expire in 2015 and will continue to expire through 2023. Our U.S. and various foreign pacritinib-directed patents expire from 2026 through 2030. Our U.S. and various foreign tosedostat-directed patents expire from 2017 to 2018.

In the absence of a patent we would, to the extent possible, need to rely on unpatented technology, know-how and confidential information. Ultimately, the lack or expiration at any given time of a patent to protect our compounds may allow our competitors to copy the underlying inventions and better compete with us.

The risks and uncertainties associated with our intellectual property, including our patents, are discussed in more detail in Part I, Item 1A, “Risk Factors”.

Manufacturing, Distribution and Associated Operations

Our manufacturing strategy utilizes third party contractors for the procurement and manufacture, as applicable, of raw materials, active pharmaceutical ingredients and finished drug product, as well as for labeling, packaging, storage and distribution of our compounds and associated supply chain operations. As our business continues to expand, we

expect that our manufacturing, distribution and related operational requirements will increase correspondingly. Additionally, in October 2016, we resumed primary responsibility for the development and commercialization of pacritinib as a result of the termination of the Pacritinib License Agreement. The development and commercialization of a major product candidate like pacritinib without a collaborative partner would significantly increase our manufacturing, distribution and related operational requirements.

Each third party contractor will always undergo a formal qualification process by CTI subject matter experts prior to signing any service agreement and initiating any manufacturing work. One item of increasing importance 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. A qualified commercial supplier for pacritinib has been identified and commercial agreement discussions are in progress.

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 compounds 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. Manufacturing facilities for products and product candidates must meet cGMP requirements, and commercialized 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 compounds in accordance with cGMPs for use in clinical trials and distribution.

We believe our operational strategy of utilizing qualified outside vendors in the foregoing manner allows us to direct our financial and managerial resources to development and commercialization activities, rather than to the establishment and maintenance of a manufacturing and distribution 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. In addition to the specific competitive factors discussed below, new anti-cancer drugs that may be developed and marketed in the future could compete with our various compounds.

With respect to PIXUVRI, while 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, 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.

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 Jakafi®, which is marketed by Incyte in the U.S., and potentially other candidates in development that target JAK inhibition to treat cancer. Tosedostat would compete with currently marketed products such as Dacogen®, Vidaza®, Revlimid®, Thalomid® and Clolar®.

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.

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. 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 European Commission 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

We are subject to extensive regulation by the FDA and other federal, state, and local regulatory agencies. The Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations set forth, among other things, requirements for the testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our products. Our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the U.S., although there can be important differences. Additionally, some significant aspects of regulation in the E.U. are addressed in a centralized way through the EMA and the European Commission, but country-specific regulation by the competent authorities of the E.U. member states remains essential in many respects.

U.S. Regulation

In the U.S., the FDA regulates drugs under the FDCA and its implementing regulations, through review and approval of NDAs. NDAs require extensive studies and submission of a large amount of data by the applicant.

Drug Development

Preclinical Testing. Before testing any compound in human subjects in the U.S., a company must generate extensive preclinical data. Preclinical testing generally includes laboratory evaluation of product chemistry and formulation, as well as toxicological and pharmacological studies in several animal species to assess the quality and safety of the product. Animal studies must be performed in compliance with the FDA's Good Laboratory Practice regulations and the U.S. Department of Agriculture's Animal Welfare Act.

IND Application. Human clinical trials in the U.S. cannot commence until an IND application is submitted and becomes effective. A company must submit preclinical testing results to the FDA as part of the IND application, and the FDA must evaluate whether there is an adequate basis for testing the drug in initial clinical studies in human volunteers. Unless the FDA raises concerns, the IND application becomes effective 30 days following its receipt by the FDA. Once human clinical trials have commenced, the FDA may stop the clinical trials by placing them on "clinical hold" because of concerns about the safety of the product being tested, or for other reasons.

Clinical Trials. Clinical trials involve the administration of the drug to healthy human volunteers or to patients, under the supervision of a qualified investigator. The conduct of clinical trials is subject to extensive regulation, including compliance with the FDA's bioresearch monitoring regulations and Good Clinical Practice, or GCP, requirements, which establish standards for conducting, recording data from and reporting the results of, clinical trials, and are intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected. Clinical trials must be conducted under protocols that detail the study objectives, parameters for monitoring safety, and the efficacy criteria, if any, to be evaluated. Each protocol is reviewed by the FDA as part of the IND application. In addition, each clinical trial must be reviewed, approved, and conducted under the auspices of an institutional review board, or IRB, at the institution conducting the clinical trial. Companies sponsoring the clinical trials, investigators, and IRBs also must comply with regulations and guidelines for obtaining informed consent from the study subjects, complying with the protocol and investigational plan, adequately monitoring the clinical trial and timely reporting adverse events. Foreign studies conducted under an IND application must meet the same requirements that apply to studies being conducted in the U.S. Data from a foreign study not conducted under an IND application may be submitted in support of an NDA if the study was conducted in accordance with GCP and the FDA is able to validate the data.

A study sponsor is required to submit certain details about active clinical trials and clinical trial results to the National Institutes of Health for public posting on http://clinicaltrials.gov. Human clinical trials typically are conducted in three sequential phases, although the phases may overlap with one another:

- Phase 1 clinical trials include the initial administration of the investigational drug to humans, typically to a small group of healthy human subjects, but occasionally to a group of patients with the targeted disease or disorder. Phase 1 clinical trials generally are intended to determine the metabolism and pharmacologic actions of the drug, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- Phase 2 clinical trials generally are controlled studies that involve a relatively small sample of the intended patient population, and are designed to develop data regarding the product's effectiveness, to determine dose response and the optimal dose range and to gather additional information relating to safety and potential adverse effects.
- Phase 3 clinical trials are conducted after preliminary evidence of effectiveness has been obtained, and are intended to gather the additional information about safety and effectiveness necessary to evaluate the drug's overall risk-benefit profile, and to provide a basis for physician labeling. Generally, Phase 3 clinical development programs consist of

expanded, large-scale studies of patients with the target disease or disorder to obtain statistical evidence of the efficacy and safety of the drug, or the safety, purity, and potency of a biological product, at the proposed dosing regimen.

The sponsoring company, the FDA or the IRB may suspend or terminate a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Further, success in early-stage clinical trials does not assure success in later-stage clinical trials. Data obtained from clinical activities are not always conclusive and may be subject to alternative interpretations that could delay, limit or prevent regulatory approval.

The FDA and IND application 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.

Drug Approval

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 there can be no assurance that any product 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 breakthrough therapy, 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 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.

In some circumstances, post-marketing testing may include post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, which are used primarily to gain additional experience from the treatment of patients in the intended population, particularly for long-term safety follow-up. In addition, the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits outweigh the risks. A REMS can include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries or other risk mitigation tools.

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. Future FDA inspections may identify compliance issues at manufacturing facilities 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. After approval in the U.S., we must comply with FDA's regulation of drug promotion and advertising, including restrictions on off-label promotion, and we comply with federal anti-kickback statutes, limitations on gifts and payments to physicians and reporting of payments to certain third-parties, among other requirements. In December 2007, we entered into a corporate integrity agreement with the Office of the Inspector General, Health and Human Services as part of our settlement agreement with the U.S. Attorney's Office 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 corporate integrity agreement, 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.

Failure to comply with applicable U.S. requirements may subject us to administrative or judicial sanctions, such as clinical holds, FDA refusal to approve pending NDAs or supplemental applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

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 the E.U., marketing authorizations for medicinal products can be obtained through several different procedures founded on the same basic regulatory process. The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products, medicinal products derived from certain biotechnological processes, advanced therapy medicinal products and certain other new medicinal products containing a new active substance for the treatment of certain diseases. It is optional for certain other products, including medicinal products that are significant therapeutic, scientific or technical innovations, or whose authorization would be in the interest of public or animal health. The centralized procedure allows a company to submit a single application to the EMA which will provide a positive opinion regarding the application if it meets certain quality, safety, and efficacy requirements. Based on the opinion of the EMA, the European Commission takes a final decision to grant a centralized marketing authorization

which is valid in all 28 E.U. Member States and three of the four European Free Trade Association states (Iceland, Liechtenstein and Norway).

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each E.U. Member State in which the product is to be marketed. One national competent authority selected by the applicant, the Reference Member State, assesses the application for marketing authorization. Following a positive opinion by the competent authority of the Reference Member State the competent authorities of the other E.U. Member States, Concerned Member States are subsequently required to grant marketing authorization for their territory on the basis of this assessment except where grounds of potential serious risk to public health require this authorization to be refused. The mutual recognition procedure is similarly based on the acceptance by the competent authorities of the Concerned Member States of the marketing authorization of a medicinal product by the competent authorities of other Reference Member States. The holder of a national marketing authorization granted by a

Reference Member State may submit an application to the competent authority of a Concerned Member State requesting that this authority mutually recognize the marketing authorization delivered by the competent authority of the Reference Member State.

Similar to accelerated approval regulations in the U.S., conditional marketing authorizations can be granted in the E.U. by the European Commission in exceptional circumstances. A conditional marketing authorization can be granted for medicinal products where a number of criteria are fulfilled; i) although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, the benefit/risk balance of the product is positive, ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data, iii) unmet medical needs will be fulfilled and iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization must be renewed annually. Under the provisions of the conditional marketing authorization for PIXUVRI, we are required to complete a post-marketing study to further investigate the effects of using PIXUVRI in patients who had received prior treatment with rituximab.

Even if a product receives authorization in the E.U., there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. Individual countries comprising the EU member states, rather than the EU, have jurisdiction across the region over patient reimbursement or pricing matters. Therefore, we will need to expend significant effort and expense to establish and maintain reimbursement arrangements in the various countries comprising the E.U. and may never succeed in obtaining widespread reimbursement arrangements therein.

The national authorities of the individual E.U. Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices and/or reimbursement of medicinal products for human use. Some E.U. Member States adopt policies according to which a specific price or level of reimbursement is approved for the medicinal product. Other E.U. Member States adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market, including volume-based arrangements and reference pricing mechanisms.

Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some E.U. Member States. These E.U. Member States include the U.K, France, Germany and Sweden. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product vary between E.U. Member States.

Post-Approval Regulation

Similarly to the U.S., both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual E.U. Member States both before and after grant of the manufacturing and marketing authorizations. Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with E.U. laws and the related national laws of individual E.U. Member States governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of marketing authorization, may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The holder of an E.U. marketing authorization for a medicinal product must also comply with E.U. pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of the marketing authorization for the product or imposition of financial penalties or other enforcement measures. In the E.U., PIXUVRI's label includes an inverted black triangle, which indicates that it is subject to additional monitoring, as a condition of authorization of PIXUVRI.

The manufacturing process for medicinal products in the E.U. is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing

authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable E.U. laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with E.U. cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the E.U. with the intention to import the active pharmaceutical ingredients into the E.U. Similarly, the distribution of medicinal products into and within the E.U. is subject to compliance with the applicable E.U. laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the E.U. Member States.

We and our third-party manufacturers are subject to cGMP, which are extensive regulations governing manufacturing processes, stability testing, record keeping and quality standards as defined by the EMA, the competent authorities of E.U. Member States and other regulatory authorities. The EMA reviews Periodic Safety Update Reports for medicinal products authorized in the E.U. If the EMA has concerns that the risk benefit profile of a product has varied, it can adopt an opinion advising that the existing marketing authorization for the product be suspended or varied and can advise that the marketing authorization holder be obliged to conduct post-authorization safety studies. The EMA opinion is submitted for approval by the European Commission. Failure by the marketing authorization holder to fulfill the obligations for which the approved opinion provides can undermine the on-going validity of the marketing authorization.

Sales and Marketing Regulations

In the E.U., the advertising and promotion of our products are subject to E.U. Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual E.U. Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the E.U.. The applicable laws at E.U. level and in the individual E.U. Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the E.U. could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

Anti-Corruption Legislation

Our business activities outside of the U.S. are subject to anti-bribery or anti-corruption laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct or rules of other countries in which we operate, including the U.K. Bribery Act of 2010.

Interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct developed at both E.U. level and in the individual E.U. Member States. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the E.U.. Violation of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain E.U. Member States also must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her competent professional organization, and/or the competent authorities of the individual E.U. Member States. Failure to comply with these requirements

could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Data Privacy and Protection

Data protection laws and regulations have been adopted at E.U. level with related implementing laws in individual E.U. Member States which impose significant compliance obligations. For example, the E.U. Data Protection Directive, as implemented into national laws by the E.U. Member States, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting.

Furthermore, there is a growth towards the public disclosure of clinical trial data in the E.U. which also adds to the complexity of processing health data from clinical trials. Such public disclosure obligations are provided in the new E.U. Clinical Trials Regulation, EMA disclosure initiatives, and voluntary commitments by industry. Data protection authorities from the different E.U. Member States may interpret the E.U. Data Protection Directive and national laws differently, which

adds to the complexity of processing personal data in the E.U., and guidance on implementation and compliance practices are often updated or otherwise revised. Failing to comply with these laws could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results. Apart from exceptional circumstances, the E.U. Data Protection Directive prohibits the transfer of personal data to countries outside of the European Economic Area, that are not considered by the European Commission to provide an adequate level of data protection, including the U.S.

Consequences of Non-Compliance

Failure to comply with applicable requirements may subject us to administrative or judicial sanctions, such as clinical holds, refusal of regulatory authorities to approve or authorize pending product applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

Environmental Regulation

In connection with our research and development activities, we are subject to federal, state and local laws, rules, regulations and policies, both internationally and domestically, governing the use, generation, manufacture, storage, air emission, effluent discharge, handling, treatment, transportation and disposal of certain materials, biological specimens and wastes and employee safety and health matters. 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 applicable law and 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 not covered by insurance could exceed our resources. See the risk factor, “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.

Employees

As of December 31, 2016, we employed 100 individuals in the U.S., including 1 employee at our majority-owned subsidiary Aequus Biopharma, Inc., or Aequus, and 4 employees in Europe. Our U.S. and U.K. employees do not have a collective bargaining agreement. One employee in Italy is subject to a collective bargaining agreement. We believe our relations with our employees are good.

Corporate Information

We were incorporated in Washington in 1991. In May 2014, we changed our name from “Cell Therapeutics, Inc.” to “CTI BioPharma Corp.” We completed our initial public offering in 1997 and our shares are listed on The NASDAQ Capital Market in the U.S. and 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.ctibiopharma.com. We may post information that is important to investors on our website. However, information found on our website is not incorporated by reference into this Annual Report on Form 10-K. “CTI BioPharma”, “PIXUVRI” and “Opaxio” are our proprietary marks. All other product names, trademarks and trade names referred to in this Annual Report on 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 Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after each is electronically filed with, or furnished to, the SEC.

In addition, you may read and copy any materials we file with the SEC 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.

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, liquidity, 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 Business, Financial Condition, Operating Results and Prospects

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

We have substantial operating expenses associated with the development of our compounds and the commercialization of PIXUVRI, and we have significant contractual payment obligations. Our available cash and cash equivalents were $44.0 million as of December 31, 2016. We believe that our present financial resources, together with payments projected to be received under certain of our contractual agreements and our ability to control costs, will only be sufficient to fund our operations into the third quarter of 2017. Cash forecasts and capital requirements are subject to change as a result of a variety of risks and uncertainties. Developments in and expenses associated with our clinical trials and other research and development activities, including the resumption of primary responsibilities for the development and commercialization of pacritinib as a result of the termination of the Pacritinib License Agreement in October 2016, acquisitions of compounds or other assets, our ability to generate projected sales of PIXUVRI, any expansion of our sales and marketing organization for PIXUVRI, regulatory approval developments, our ability to consummate appropriate collaborations for development and commercialization activities, our ability to reach milestones triggering payments under applicable contractual arrangements, receive the associated payments, litigation and other disputes, competitive market developments and other unplanned expenses or business developments may consume capital resources earlier than planned. Due to these and other factors, any 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.

As of December 31, 2016, we had an outstanding principal balance under our senior secured term loan agreement of $19.5 million. We were required to make monthly interest-only payments in respect thereof in the approximate amount of $0.2 million until March 31, 2016. Following March 31, 2016, we are required to make monthly interest plus principal payments through December 1, 2018 in the approximate amount of $0.8 million, with the final principal payment of approximately $3.3 million on December 1, 2018. These borrowings are secured by a first priority security interest on substantially all of our personal property except our intellectual property and subject to certain other exceptions. In addition, the senior secured term loan agreement 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 will need to raise additional funds to operate our business. We may seek to raise such capital through public or private equity financings, partnerships, collaborations, joint ventures, disposition of assets, debt financings or restructurings, bank borrowings or other sources of financing. However, our ability to do so is subject to a number of risks, uncertainties, constraints and consequences, including, but not limited to, the following:

- 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 potential difficulty of obtaining shareholder approval to increase authorized shares and the restrictive covenants under our senior secured term loan agreement;
- issuance of equity-based securities will dilute the proportionate ownership of existing shareholders;
- our ability to obtain further funds from any potential loan arrangements is limited by our existing senior secured term loan agreement;
- certain financing arrangements may require us to relinquish rights to various assets and/or impose more restrictive terms than any of our existing or past arrangements; 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.

For these and other reasons, 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, be unable to attract and retain highly qualified personnel, refrain from making our contractually required payments when due (including debt payments) and/or be forced to cease operations, liquidate our assets and possibly seek bankruptcy protection. Any of these consequences could harm our business, financial condition, operating results and prospects.

We may not be able to maintain our listings on The NASDAQ Capital Market and the Mercato Telematico Azionario, or 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 and consequently may negatively impact the price of our common stock.

On March 22, 2016, we received a notification from The NASDAQ Stock Market LLC, or NASDAQ, indicating that we would be delisted if we do not regain compliance with the minimum $1.00 per share closing bid price of our common stock required for continued listing of our common stock on The NASDAQ Capital Market under NASDAQ Listing Rule 5550(a)(2). We subsequently regained compliance with the minimum bid price requirement by effecting a 1-for-10 reverse stock split. However, there can be no assurance that we will be able to comply with the continued listing standards in the future.

If our common stock ceases to be listed for trading on The NASDAQ Capital Market for failure to regain compliance with the minimum $1.00 per share closing bid price requirement or for any other 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 market 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 in Italy. 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, CONSOB 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 market price of our common stock.

Our audit report for the year ended December 31, 2016 contains an explanatory paragraph on our consolidated financial statements, and we may in the future, receive additional such reports.

Our independent registered public accounting firm included an explanatory paragraph in its reports on our consolidated financial statements for the year ended December 31, 2016 regarding their substantial doubt as to our ability to continue as a

going concern. We believe that our present financial resources, together with payments projected to be received under certain contractual agreements and our ability to control costs, will only be sufficient to fund our operations into the third quarter of 2017, which does raise substantial doubt about our ability to continue as a going concern. The inclusion of a going concern explanatory paragraph in our audit report for the year ended December 31, 2016 and for 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 expect to 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, 2016, we had an accumulated deficit of $2.2 billion, and we expect to continue to incur net losses. As part of our business plan, we will need to continue to conduct research, development, testing and regulatory compliance activities with respect to our compounds and ensure the procurement of manufacturing and drug supply services, the costs of which, together with projected general and administrative expenses, is expected to result in operating losses for the foreseeable future. There can be no assurances that we will ever achieve profitability.

In order to develop and commercialize pacritinib, we will need to raise additional financing or seek a new collaboration partner for pacritinib.

We have resumed primary responsibility for the development and commercialization of pacritinib as a result of the termination of the Pacritinib License Agreement in October 2016, and we will no longer be eligible to receive cost sharing or milestone payments for pacritinib's development from Baxalta. Because obtaining regulatory approval requires substantial time, effort and financial resources, the termination of this collaborative partnership could negatively impact our ability to successfully develop and commercialize pacrtinib. We currently have no commitments or arrangements for any additional financing to fund the development and commercial launch of pacritinib, and we will need to seek additional funding, which may not be available or may not be available on favorable terms. We could also seek another collaborative partnership for the development and commercialization of pacritinib, which may not be available on reasonable terms or at all.

If our development and commercialization collaborations are not successful, or if we are unable to enter into additional collaborations, we may not be able to effectively develop and/or commercialize our compounds, which could have a material adverse effect on our business.

Our business is heavily dependent on the success of our development and commercialization collaborations. In particular, under the Servier Agreement, we rely heavily on Servier to collaborate with us to develop and commercialize PIXUVRI. As a result of our dependence on our relationship with Servier, the success or commercial viability of PIXUVRI 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 Servier, including the following: possible disagreements as to the timing, nature and extent of development plans for the respective compound, including clinical trials or regulatory approval strategy; changes in their respective personnel who are key to the collaboration efforts; any changes in their respective business strategies adverse to our interests, whether in connection with a change of control or otherwise; possible disagreements regarding ownership of proprietary rights; the ability to meet our financial and other contractual obligations under the respective agreements; and the possibility that Servier could elect to terminate their agreement with us pursuant to "at-will" termination clauses or breach their agreement with us. Furthermore, the contingent financial returns under our collaboration with Servier depends in large part on the achievement of development and commercialization milestones and the ability to generate applicable product sales to trigger royalty payments. Therefore, our success, and any associated future financial returns to us and our investors, will depend in large part on the performance of Servier. If our existing collaborations fail, or if we do not successfully

enter into additional collaborations when needed, we may be unable to further develop and commercialize the applicable compounds, generate revenues to sustain or grow our business or achieve profitability, which would harm our business, financial condition, operating results and prospects.

The regulatory approval process for pacritinib has been subject to delay and uncertainty associated with clinical holds placed on pacritinib clinical trials in February 2016 and the planned withdrawal of the MAA in Europe. While the full clinical hold on pacritinib trials has been removed and we plan to submit a new MAA in the second quarter of 2017, our planned dose-exploration trial for pacritinib and further clinical trials for pacritinib could be subject to further delay or we could be prevented from further studying pacritinib or seeking its commercialization.

On February 8, 2016, the FDA notified us that a full clinical hold had been placed on pacritinib and we subsequently withdrew our NDA for pacritinib until we determine next steps. A full clinical hold is a suspension of the clinical work requested under an investigational new drug application. Under the full clinical hold, all patients currently on

pacritinib were required to discontinue pacritinib, and we are not permitted to enroll any new patients or start pacritinib as initial or crossover treatment. In its written notification, the FDA noted interim overall survival results from PERSIST-2 showing a detrimental effect on survival consistent with the results from PERSIST-1, and that deaths in PERSIST-2 in pacritinib-treated patients include intracranial hemorrhage, cardiac failure and cardiac arrest. On January 3, 2017, the full clinical hold was removed. Our complete response submission included, among other items, final Clinical Study Reports for both PERSIST-1 and 2 trials and the dose-exploration clinical trial protocol requested by the FDA. We plan to start the new trial, PAC203, in the second quarter of 2017 and enroll up to approximately 105 patients with primary myelofibrosis who have failed prior ruxolitinib therapy to evaluate the dose response relationship for safety and efficacy (spleen volume reduction at 12 or 24 weeks) of three dose regimens: 100 mg once-daily, 100 mg twice-daily (BID) and 200 mg BID. The 200 mg BID dose regimen was used in PERSIST-2. The results of PAC203 may not address all of the FDA's concerns regarding appropriate safe and efficacious dosage for pacritinib, and the FDA may again request additional information or require us to pursue new clinical safety trials with changes to, among other things, protocol, study design or sample size.

Further, in the EMA's initial assessment report regarding our MAA, the CHMP determined that the current application is not approvable because of major objections in the areas of efficacy, safety (hematological and cardiovascular toxicity) and the overall risk-benefit profile of pacritinib. Subsequent to the filing of the MAA, data from the second phase 3 trial of pacritinib, PERSIST-2, were reported. These data suggest that pacritinib may show clinical benefit in patients who have failed or are intolerant to ruxolinitib therapy, a population for which there is no approved therapy. Following discussions with the EMA about how PERSIST-2 data might address the major objections and how to integrate the data into the current application, we have decided to withdraw the MAA. We are preparing a new MAA that seeks to address the major objections by including data from PERSIST-2. The new application will focus on patients who have failed or are intolerant to ruxolitinib. We plan to submit this new application in the second quarter of 2017.

The submission of new marketing applications, complying with any additional requests for information from the FDA or EMA or making any changes to protocol, study design, or sample size may be time-consuming, expensive and delay or prevent our ability to continue to study pacritinib. If we are unable to address any further recommendations and requests or the EMA's major objections in a manner satisfactory to the FDA or EMA, as applicable, in a timely manner, or at all, we could be delayed or prevented from seeking commercialization of pacritinib. Delays in the commercialization of pacritinib would prevent us from receiving future milestone or royalty payments, and otherwise significantly harm our business.

Compounds that appear promising in research and development may fail to reach later stages of development for a number of reasons, including, among others, that clinical trials may take longer to complete than expected or may not be completed at all, and top-line or preliminary clinical trial data reports may ultimately differ from actual results once existing data are more fully evaluated.

Successful development of anti-cancer and other pharmaceutical products is highly uncertain, and obtaining regulatory approval to market drugs to treat cancer is expensive, difficult and speculative. Compounds that appear promising in research and development may fail to reach later stages of development for several reasons, including, but not limited to:

- delay or failure in obtaining necessary U.S. and international regulatory approvals, or the imposition of a partial or full regulatory hold on a clinical trial;

- difficulties in formulating a compound, scaling the manufacturing process, timely attaining process validation for particular drug products and obtaining manufacturing approval;

- pricing or reimbursement issues or other factors that may make the product uneconomical to commercialize;

- production problems, such as the inability to obtain raw materials or supplies satisfying acceptable standards for the manufacture of our products, equipment obsolescence, malfunctions or failures, product quality/contamination problems or changes in regulations requiring manufacturing modifications;

- inefficient cost structure of a compound compared to alternative treatments;

- obstacles resulting from proprietary rights held by others with respect to a compound, such as patent rights;

- lower than anticipated rates of patient enrollment as a result of factors, such as the number of patients with the relevant conditions, the proximity of patients to clinical testing centers, eligibility criteria for tests and competition with other clinical testing programs;

- preclinical or clinical testing requiring significantly more time than expected, resources or expertise than originally expected and inadequate financing, which could cause clinical trials to be delayed or terminated;

- failure of clinical testing to show potential products to be safe and efficacious, and failure to demonstrate desired safety and efficacy characteristics in human clinical trials;

- suspension of a clinical trial at any time by us, an applicable collaboration partner or a regulatory authority on the basis that the participants are being exposed to unacceptable health risks or for other reasons;

- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs, and trial sites; and

- failure of third parties, such as CROs, academic institutions, collaborators, cooperative groups and/or investigator sponsors, to conduct, oversee and monitor clinical trials and results.

In addition, from time to time we report top-line data for clinical trials. Such data are based on a preliminary analysis of then-available efficacy and safety data, and such findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. Top-line or preliminary data are based on important assumptions, estimations, calculations and information then available to us to the extent we have had, at the time of such reporting, an opportunity to fully and carefully evaluate such information in light of all surrounding facts, circumstances, recommendations and analyses. As a result, top-line results may differ from future results, or different conclusions or considerations may qualify such results once existing data have been more fully evaluated. In addition, third parties, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular compound and our business in general.

If the development of our compounds is delayed or fails, or if top-line or preliminary clinical trial data reported differ from actual results, our development costs may increase and the ability to commercialize our compounds 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 develop or commercialize some or all of our compounds.

We are subject to rigorous and extensive regulation by the FDA in the U.S. and by comparable agencies in other jurisdictions, including the EMA in the E.U. Some of our other product candidates 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 our compounds. 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 jurisdictions until they have received approval from the appropriate foreign regulatory 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. For instance, on February 8, 2016, the FDA placed pacritinib on full clinical hold and the clinical hold was not removed until January 3, 2017. The number, size, design and focus of preclinical and clinical trials that will be required for approval by the FDA, the EMA or any other foreign regulatory agency varies depending on the compound, the disease or condition that the compound is designed to address and the regulations applicable to any particular compound. 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 compound for many reasons, including, but not limited to:

- a compound may not be shown to be safe or effective;

- the clinical and other benefits of a compound may not outweigh its safety risks;
- clinical trial results may be negative or inconclusive, or adverse medical events may occur during a clinical trial;
- the results of clinical trials may not meet the level of statistical significance required by regulatory agencies for approval;
- such regulatory agencies may interpret data from pre-clinical and clinical trials in different ways than we do;

- such regulatory agencies may not approve the manufacturing process of a compound or determine that a third party contract manufacturers manufactures a compound in accordance with current good manufacturing practices, or cGMPs;

- a compound may fail to comply with regulatory requirements; or

- such regulatory agencies might change their approval policies or adopt new regulations.

If our compounds are not approved at all or quickly enough to provide net revenues to defray our operating expenses, our business, financial condition, operating results and prospects could be harmed.

In the event that we seek and the FDA does not grant accelerated approval or priority review for a drug candidate, we would experience a longer time to commercialization in the U.S., if commercialized at all, our development costs may increase and our competitive position may be harmed.

We were seeking accelerated approval and requested Priority Review of our NDA for pacritinib. However, on February 8, 2016, the FDA notified us that a full clinical hold had been placed on pacritinib and we subsequently withdrew our NDA for pacritinib. On January 3, 2017, the full clinical hold was removed, and we now intend to conduct a new trial, PAC203, that plans to enroll up to approximately 105 patients with primary myelofibrosis who have failed prior ruxolitinib therapy to evaluate the dose response relationship for safety and efficacy (spleen volume reduction at 12 and 24 weeks) of three dose regimens: 100 mg once-daily, 100 mg twice-daily (BID) and 200 mg BID. The 200 mg BID dose regimen was used in PERSIST-2.

We may in the future decide to seek accelerated approval pathway for our compounds. The FDA may grant accelerated approval to a product designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. A surrogate endpoint under an accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. There can be no assurance that the FDA will agree that any endpoint we suggest with respect to any of our drug candidates is an appropriate surrogate endpoint. Furthermore, there can be no assurance that any application will be accepted or that approval will be granted. Even if a product candidate is granted accelerated approval, such accelerated approval is contingent on the sponsor's agreement to conduct one or more post-approval confirmatory trials. Such confirmatory trial(s) must be completed with due diligence and, in some cases, the FDA may require that the trial(s) be designed and/or initiated prior to approval. Moreover, the FDA may withdraw approval of a product candidate or indication approved under the accelerated approval pathway for a variety of reasons, including if the trial(s) required to verify the predicted clinical benefit of a product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug, or if the sponsor fails to conduct any required post-approval trial(s) with due diligence.

In the event of priority review, the FDA has a goal to (but is not required to) take action on an application within a total of eight months (rather than a goal of twelve months for a standard review). The FDA grants priority review only if it determines that a product treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness when compared to a standard application. The FDA has broad discretion whether to grant priority review, and, while the FDA has granted priority review to other oncology product candidates, our drug candidates may not receive similar designation. Moreover, receiving priority review from the FDA does not guarantee completion of review or approval within the targeted eight-month cycle or thereafter.

A failure to obtain accelerated approval or priority review would result in a longer time to commercialization of the applicable compound in the U.S., if commercialized at all, could increase the cost of development and could harm our competitive position in the marketplace.

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

The development and ongoing clinical trials for our compounds may not be successful and, even if they are, the resulting products may never be successfully developed into commercial products. Even if we are successful in our clinical trials and in obtaining other regulatory approvals, the respective products may not reach or remain in 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 experience excessive product loss due to contamination, equipment failure, inadequate transportation or storage, improper installation or operation of equipment, vendor or operator error, inconsistency in yields or variability in product characteristics;
- they may be uneconomical to produce;
- political and legislative changes emerging after the recent election of the President of the United States may make the commercialization of our product candidates more difficult;
- we may fail to obtain reimbursement approvals or pricing that is cost effective for patients as compared to other available forms of treatment or that covers the cost of production and other expenses;
- they may not compete effectively with existing or future alternatives;
- we may be unable to develop commercial operations and to sell marketing rights;
- they may fail to achieve market acceptance; or
- we may be precluded from commercialization of a product due to proprietary rights of third parties.

In particular, with respect to the commercialization of PIXUVRI, we will be heavily dependent on our collaboration partner, Servier. The failure of Servier (or any other applicable collaboration partner) to fulfill its commercialization obligations with respect to a compound, or the occurrence of any of the events in the list above, could adversely affect the commercialization of our products. Additionally, uncertainty and speculation regarding the possible repeal of all or a portion of the Patient Protection and Affordable Care Act has emerged after the recent election of the President of the United States. Members of the Trump administration, including the President, have made statements suggesting the administration plans to seek repeal of all or portions of the Affordable Care Act, and have stated that they will ask Congress to replace the current legislation with new legislation. The uncertainty this causes for the healthcare industry could also 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.

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

To the extent our products are developed, commercialized and successfully introduced to market, they may not be considered cost-effective and third party or government reimbursement might not be available or sufficient. Globally,

governmental and other third party payors are becoming increasingly aggressive in attempting to contain health care costs by strictly controlling, directly or indirectly, pricing and reimbursement and, in some cases, limiting or denying coverage altogether on the basis of a variety of justifications, and we expect pressures on pricing and reimbursement from both governments and private payors inside and outside the U.S. to continue. In the U.S., we are subject to substantial pricing, reimbursement and access pressures from state Medicaid programs, private insurance programs and pharmacy benefit managers, and implementation of U.S. health care reform legislation is increasing these pricing pressures. The Patient Protection and Affordable Care Act instituted comprehensive health care reform, which includes provisions that, among other things, reduce and/or limit Medicare reimbursement, require all individuals to have health insurance (with limited exceptions) and impose new and/or increased taxes. In addition, members of the Trump administration, including the President, have made public statements criticizing pricing practices within the pharmaceutical industry, indicating that they may seek to increase pricing pressures on the pharmaceutical industry.

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. Reimbursement decisions from one or more of the European markets may impact reimbursement decisions in other European markets. 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. The continuing efforts of government and insurance companies, health maintenance organizations and other payors of health care costs to contain or reduce costs of health care may affect our future revenues and profitability or those of our potential customers, suppliers and collaborative partners, as well as 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, in part, on our ability and that of our collaborator, Servier, to successfully commercialize our only currently marketed product, PIXUVRI. PIXUVRI is not approved for marketing in the U.S., is presently available only in a limited number of countries and is reimbursed in even fewer countries.

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

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

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

Post-approval or authorization regulatory reviews and obligations often result in significant expense and marketing limitations, and any failure to satisfy such ongoing obligations, including, in particular, our post-authorization commitment trial for PIXUVRI, could negatively affect our business, financial condition, operating results or prospects.

Even if a product receives regulatory approval or authorization, as applicable, we are and will continue to be subject to numerous regulations and statutes regulating the manner of obtaining reimbursement for and selling the product, including limitations on the indicated uses for which a product may be marketed. Approved or authorized products, including PIXUVRI, are subject to extensive manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping regulations. These requirements include submissions of safety and other post-marketing information and reports. In addition, such products are subject to ongoing maintenance of product registration and continued compliance with cGMPs, good clinical practices, or GCPs, and good laboratory practices,

or GLPs. Further, distribution of products must be conducted in accordance with good distribution practices, or GDPs. The distribution process and facilities of our third party distributors are subject to, and our wholesale distribution authorization by the UK Medicines and Healthcare Products Regulatory Agency subjects us to, continuing regulation by applicable regulatory authorities with respect to the distribution and storage of products. Regulatory authorities may also impose new restrictions on continued product marketing or may require the withdrawal of a product from the market if adverse events of unanticipated severity or frequency are discovered following approval. In addition, regulatory agencies may impose post-approval/post-authorization clinical trials, such as our ongoing PIX306 trial of PIXUVRI required by the EMA. We cannot predict the outcome of PIX306 or whether we will be able to complete the associated requirements in a timely manner. If we are unable to submit the requisite PIX306 clinical study report by the due date in December 2018 and are unable to obtain an extension of such deadline, or if we are otherwise unable to satisfy all applicable requirements, our conditional marketing authorization for PIXUVRI may be revoked.

Any other failure to comply with applicable regulations could result in warning or untitled letters, product recalls, interruption of manufacturing and commercial supply processes, withdrawal or seizure of products, suspension of an applicable wholesale distribution authorization and/or distribution of products, operating restrictions, injunctions, suspension of licenses, revocation of the applicable product's approval or authorization, other administrative or judicial sanctions (including civil penalties and/or criminal prosecution) and/or unanticipated related expenditure to resolve shortcomings, which could negatively affect our business, financial condition, operating results or prospects.

We may be unable to obtain a quorum for meetings of our shareholders or obtain requisite shareholder approval and, consequently, be unable to take certain corporate actions, including financing activities.

Failure to meet the requisite quorum or obtain requisite shareholder approval can prevent us from raising capital through equity financing or otherwise taking certain actions that may be in our best interest and that of our shareholders. We have experienced such difficulties in the past.

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% 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, 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% 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 applicable rules and regulations, particularly in light of difficulties we have had in the past in obtaining a quorum and obtaining the requisite vote. If we are unable to obtain financing or our financing options are limited due to shareholder approval difficulties, such failure may harm our ability to continue operations.

Additionally, a portion 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 recent years, certain depository banks in Italy holding shares of our common stock have facilitated book-entry transfers of their share positions at Monte Titoli, S.p.A., the Italian central clearing agency, to their U.S. 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 we contacted to facilitate these arrangements agreed to make the share transfers pursuant to these arrangements as of the record date of the shareholder 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 may 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 do so in the future.

As a result of the foregoing or for other reasons, we may be unable to obtain a quorum 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. Any failure to obtain a quorum or the requisite vote on a proposal in question could harm us.

We are subject to Italian regulatory requirements, which limit our ability to issue additional shares of our common stock, could result in administrative and other challenges and additional expenses and/or could limit our ability to undertake other business initiatives.

Because our common stock is traded on the MTA in Italy, we are required to also comply with the rules and regulations of the Commissione Nazionale per le Società e la Borsa , or CONSOB, and the Borsa Italiana S.p.A., or Borsa Italiana, which regulate companies listed on Italy's public markets. 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 (which jointly compose a prospectus) that have to be approved by CONSOB prior to issuing common stock that is equal to or exceeds, in any twelve-month period, 10% 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 issued convertible preferred stock in numerous prior offerings and may in the future issue convertible securities; 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% limitation imposed by E.U. and Italian law. However, this exception to the prospectus requirement could change or cease to be available as a result of changes in regulations, interpretive positions, and policies or otherwise. Any such change may increase compliance costs or limit our ability to issue securities. 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 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 and fines or other sanctions from time to time. For more information on a current investigation, see Part I, Item 3. "Legal Proceedings".

Any of such regulatory requirements of CONSOB and the Borsa Italiana could result in administrative and other challenges and additional expenses, limit our ability to undertake other business initiatives and negatively affect our business, financial condition, operating results and prospects.

We will incur a variety of costs for, and may never realize the anticipated benefits of, acquisitions, collaborations or other strategic transactions.

We evaluate and undertake acquisitions, collaborations and other strategic transactions from time to time. The process of negotiating these transactions, as well as integrating any acquisitions and implementing any strategic alliances, may result in operating difficulties and expenditures. In addition, these transactions 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. These undertakings could also result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or amortization expenses related to intangible assets, and we may never realize the anticipated benefits. In addition, following the consummation of a transaction, our results of operations and the market price of our common stock may be affected by factors different from those that affected our results of operations and the market price of our common stock prior to such acquisition. Any of the foregoing consequences resulting from transactions of the type described above could harm our business, financial condition, operating results or prospects.

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, ultimate sale and use 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. 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 the numerous laws and regulations that govern our business, including those related to cross-border conduct, health care fraud and abuse, anti-corruption and false claims and the protection of health information, 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 Practices Act, or the FCPA, the U.K. Bribery Act 2010 and other anti-corruption laws. These laws 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 products. 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 health care 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 may also be subject to the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act and their respective implementing regulations, or HIPAA, which established uniform standards for certain “covered entities” (health care providers, health plans and health care clearinghouses) governing the conduct of certain electronic health care transactions and protecting the security and privacy of protected health information. Among other things, HIPAA’s privacy and security standards are directly applicable to “business associates” - independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. In addition to possible civil and criminal penalties for violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney’s fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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 applicable laws or regulations, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government health care 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 party service providers for a number of critical operational activities including, in particular, for the manufacture, testing and distribution of our compounds and associated supply chain operations, as well as for clinical trial activities. Any failure or delay in these undertakings by third parties could harm our business.

Our business is dependent on the performance by third parties of their responsibilities under contractual relationships. In particular, we rely heavily on third parties for the manufacture and testing of our compounds. We do not have internal analytical laboratory or manufacturing facilities to allow the testing or production of compounds in compliance with GLP and cGMP. As a result, we rely on third parties to supply us in a timely manner with manufactured products/product candidates. We may not be able to adequately manage and oversee the manufacturers we choose, they may not perform as agreed or they may terminate their agreements with us. In particular, we depend on third party manufacturers to conduct their operations in compliance with GLP and cGMP or similar standards imposed by the U.S. and/or applicable foreign regulatory authorities, including the FDA and EMA. Any of these regulatory authorities may take action against a contract manufacturer who violates GLP and cGMP. 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.

We may not be able to obtain sufficient quantities of our compounds if we are unable to secure manufacturers when needed, or if our designated manufacturers do not have the capacity or otherwise fail to manufacture compounds according to our schedule and specifications or fail to comply with cGMP regulations. In particular, in connection with the transition of the manufacturing of PIXUVRI and pacritinib drug supply to successor vendors, respectively, we could face logistical, scaling or other challenges that may adversely affect supply. Furthermore, in order to ultimately obtain and maintain applicable regulatory approvals, any manufacturers we utilize are required to consistently produce the respective compounds in commercial quantities and of specified quality or execute fill-finish services on a repeated basis and document their ability to do so, which is referred to as process validation. In order to obtain and maintain regulatory approval of a compound, the applicable regulatory authority must consider the result of the applicable process validation to be satisfactory and must otherwise approve of the manufacturing process. Even if

our compound manufacturing processes obtain regulatory approval and sufficient supply is available to complete clinical trials necessary for regulatory approval, there are no guarantees we will be able to supply the quantities necessary to effect a commercial launch of the applicable drug, or once launched, to satisfy ongoing demand. Any compound shortage could also impair our ability to deliver contractually required supply quantities to applicable collaborators, as well as to complete any additional planned clinical trials.

We also rely on third party service providers for certain warehousing, transportation, sales, order processing, distribution and cash collection services. With regard to the distribution of our compounds, we depend on third party distributors to act in accordance with GDP, and the distribution process and facilities are subject to continuing regulation by applicable regulatory authorities with respect to the distribution and storage of products.

In addition, we depend on medical institutions and CROs (together with their respective agents) to conduct clinical trials and associated activities in compliance with GCP and in accordance with our timelines, expectations and requirements. To the

extent any such third parties are delayed in achieving or fail to meet our clinical trial enrollment expectations, fail to conduct our trials in accordance with GCP or study protocol or otherwise take actions outside of our control or without our consent, our business may be harmed. Furthermore, we conduct clinical trials in foreign countries, subjecting us to additional risks and challenges, including, in particular, as a result of the engagement of foreign medical institutions and foreign CROs, who may be less experienced with regard to regulatory matters applicable to us and may have different standards of medical care.

With regard to certain of the foregoing clinical trial operations and stages in the manufacturing and distribution chain of our compounds, we rely on single vendors. In particular, our current business structure contemplates, at least in the foreseeable future, use of a single commercial supplier for PIXUVRI drug substance. In addition, in the event pacritinib is approved, we are initially preparing to have only one commercial supplier for pacritinib. We may in the future seek to qualify an additional manufacturer of pacritinib, but the process for qualifying a manufacturer can be lengthy and may not occur on a timely basis or at all. The use of single vendors for core operational activities, such as clinical trial operations, manufacturing and distribution, and the resulting lack of diversification, expose us to the risk of a material interruption in service related to these single, outside vendors. As a result, our exposure to this concentration risk could harm our business.

Although we monitor the compliance of our third party service providers performing the aforementioned services, we cannot be certain that such service providers will consistently comply with applicable regulatory requirements or that they will otherwise timely satisfy their obligations to us. Any such failure and/or any failure by us to monitor their services and to plan for and manage our short and long term requirements underlying such services could result in shortage of the compound, delays in or cessation of clinical trials, failure to obtain or revocation of product approvals or authorizations, product recalls, withdrawal or seizure of products, suspension of an applicable wholesale distribution authorization and/or distribution of products, operating restrictions, injunctions, suspension of licenses, other administrative or judicial sanctions (including civil penalties and/or criminal prosecution) and/or unanticipated related expenditures to resolve shortcomings. Such consequences could have a significant impact on our business, financial condition, operating results or prospects.

If we are unable to recruit, retain, integrate and motivate senior management, other key personnel and directors, or if such persons are unable to perform effectively, our business could suffer.

Our future success depends, in part, on our ability to continue to attract and retain senior management, other key personnel and directors to enable the execution of our business plan and to identify and pursue new opportunities. Additionally, our productivity and the quality of our operations are dependent on our ability to integrate and train our new personnel quickly and effectively. In February 2017, we announced the appointment of Adam Craig, M.D., Ph.D., as President and Chief Executive Officer effective March 20, 2017. Leadership transitions and management changes can be difficult to manage and may create uncertainty or disruption to our business or increase the likelihood of turnover in our other officers and employees. We may not be able to effectively manage our transition to a new president and chief executive officer.

Directors and management of publicly traded corporations are increasingly concerned with the extent of their personal exposure to lawsuits and shareholder claims, as well as governmental, creditor and other claims that may be made against them. Due to these and other reasons, such persons are also becoming increasingly concerned with the availability of directors and officers liability insurance to pay on a timely basis the costs incurred in defending such claims. We currently carry directors and officers liability insurance. However, directors and officers liability insurance is expensive and can be difficult to obtain. If we are unable to continue to provide directors and officers sufficient liability insurance at affordable rates or at all, or if directors and officers perceive our ability to do so in the future to be limited, it may become increasingly more difficult to attract and retain management and qualified directors to serve on our Board of Directors.

The loss of the services of senior management, other key personnel or directors and/or the inability to timely attract or integrate such persons could significantly delay or prevent the achievement of our development and strategic objectives and may adversely affect our business, financial condition and operating results.

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 ibrutinib, idelalisib, lenolidimide,

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.

- If we are successful in bringing pacritinib to market, pacritinib will face competition from the currently approved JAK1/JAK2 inhibitor, Jakafi®.

- If we are successful in bringing tosedostat to market, we will face competition from currently marketed products, such as cytarabine, Dacogen®, Vidaza®, Clolar®, Revlimid® and Thalomid®.

In addition to the specific competitive factors discussed above, new anti-cancer drugs that may be under development or developed and marketed in the future could compete with our various compounds.

Many of our competitors, particularly 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, commercializing, manufacturing, marketing and selling products. As a result, products of our competitors might come to market sooner or 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 PIXUVRI or any potential future product would likely suffer and we might never recoup the significant investments we have made and will continue to make to develop and market these compounds.

If any of our license agreements for intellectual property underlying our compounds are terminated, we may lose the right to develop or market that product.

We have acquired or licensed intellectual property from third parties, including patent applications and patents relating to intellectual property for PIXUVRI, pacritinib and tosedostat. Some of our product development programs depend on our ability to maintain rights under these arrangements. Each licensor has the power to terminate its agreement with us if we fail to meet our obligations under these licenses. We may not be able to meet our obligations under these licenses. If we default under any license agreement, we may lose our right to market and sell any products based on the licensed technology and may be forced to cease operations, liquidate our assets and possibly seek bankruptcy protection. Bankruptcy may result in the termination of agreements pursuant to which we license certain intellectual property rights.

If we are unable to in-license or acquire additional product candidates, our future product portfolio and potential profitability could be harmed.

One component of our business strategy is the in-licensing and acquisition of drug compounds developed by other pharmaceutical and biotechnology companies or academic research laboratories. PIXUVRI, pacritinib and tosedostat have all been in-licensed or acquired from third parties. Competition for new promising compounds and commercial products can be intense. If we are not able to identify future in-licensing or acquisition opportunities and enter into arrangements on acceptable terms, our future product portfolio and potential profitability could be harmed.

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 of these patents may allow our competitors to copy the inventions that are currently protected.

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 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.

Our PIXUVRI-directed patents currently in force in Europe began to expire in late March 2015 and will continue to expire through a portion of 2023. Some of these European patents are also subject to Supplementary Protection Certificates such that the extended patents will expire from 2020 to 2027. In the United States, our PIXUVRI-directed U.S. patent will expire in 2024. Our PIXUVRI-directed patents outside of Europe and the U.S. began to expire in 2015 and will continue to expire through 2023.

Our U.S. and various foreign pacritinib-directed patents expire from 2026 through 2030. Our U.S. and various foreign tosedostat-directed patents expire from 2017 to 2018.

In the absence of a patent, we would, to the extent possible, need to rely on unpatented technology, know-how and confidential information. Ultimately, the lack or expiration at any given time of a patent to protect our compounds may allow our competitors to copy the underlying inventions and better compete with us.

If we fail to adequately protect our intellectual property, our competitive position and the potential for long-term success could be harmed.

Development and protection of our intellectual property are critical to our business. If we do not adequately protect our intellectual property, competitors may be able to practice our technologies. Our success depends in part on our ability to:

•obtain and maintain patent protection for our products or processes both in the U.S. and other countries;
•protect trade secrets; and
•prevent others from infringing on our proprietary rights.

The patent position of pharmaceutical and biotechnology firms, including ours, generally is highly uncertain and involves complex legal and factual questions. The U.S. Patent and Trademark Office has not established a consistent policy regarding the breadth of claims that it will allow in biotechnology patents. If it allows broad claims, the number and cost of patent interference proceedings in the U.S. and the risk of infringement litigation may increase. If it allows narrow claims, the risk of infringement may decrease, but the value of our rights under our patents, licenses and patent applications may also decrease. Patent applications in which we have rights may never issue as patents, and the claims of any issued patents may not afford meaningful protection for our technologies or products. In addition, patents issued to us or our licensors may be challenged and subsequently narrowed, invalidated or circumvented. Litigation, interference proceedings or other governmental proceedings that we may become involved in with respect to our proprietary technologies or the proprietary technology of others could result in substantial cost to us.

We also rely upon trade secrets, proprietary know-how and continuing technological innovation to remain competitive. Third parties may independently develop such know-how or otherwise obtain access to our technology. While we require our employees, consultants and corporate partners with access to proprietary information to enter into confidentiality agreements, these agreements may not be honored.

Patent litigation is widespread in the biotechnology industry, and any patent litigation could harm our business.

Costly litigation might be necessary to protect a patent position or to determine the scope and validity of third party proprietary rights, and we may not have the required resources to pursue any such litigation or to protect our patent rights. Any adverse outcome in litigation with respect to the infringement or validity of any patents owned by third parties could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using a product or technology. With respect to our in-licensed patents, if we attempt to initiate a patent infringement suit against an alleged infringer, it is possible that our applicable licensor will not participate in or assist us with the suit and as a result we may not be able to effectively enforce the applicable patents against the alleged infringers.

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.

At times, we may monitor patent filings for patents that might be relevant to some of our products and product candidates in an effort to guide the design and development of our products to avoid infringement, but may not have conducted an exhaustive search. We may not be able to successfully challenge the validity of third party patents and could be required to pay substantial damages, possibly including treble damages, for past infringement and attorneys' fees if it is ultimately determined that our products infringe such patents. Further, we may be prohibited from selling our products before we obtain a license, which, if available at all, may require us to pay substantial royalties.

Moreover, third parties may challenge the patents that have been issued or licensed to us. We do not believe that PIXUVRI, pacritinib or any of the other compounds we are currently developing infringe upon the rights of any third parties nor are they materially infringed upon by third parties; however, there can be no assurance that our technology will not be found in the future to infringe upon the rights of others or be infringed upon by others. In such a case, others may assert infringement claims against us, and should we be found to infringe upon their patents, or otherwise impermissibly utilize their

intellectual property, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties' patent rights. In addition to any damages we might have to pay, we may be required to obtain licenses from the holders of this intellectual property, enter into royalty agreements or redesign our compounds so as not to utilize this intellectual property, each of which may prove to be uneconomical or otherwise impossible. Conversely, we may not always be able to successfully pursue our claims against others that infringe upon our technology and the technology exclusively licensed from any third parties. Thus, the proprietary nature of our technology or technology licensed by us may not provide adequate protection against competitors.

Even if infringement claims against us are without merit, or if we challenge the validity of issued patents, lawsuits take significant time, may, even if resolved in our favor, be expensive and divert management attention from other business concerns. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations.

The illegal distribution and sale by third parties of counterfeit versions of a product or stolen product could have a negative impact on our reputation and business.

Third parties might illegally distribute and sell counterfeit or unfit versions of a product that do not meet our rigorous manufacturing and testing standards. A patient who receives a counterfeit or unfit product may be at risk for a number of dangerous health consequences. Our reputation and business could suffer harm as a result of counterfeit or unfit product sold under our brand name. In addition, thefts of inventory at warehouses, plants or while in-transit, which are not properly stored and which are sold through unauthorized channels, could adversely impact patient safety, our reputation and our business.

We may owe additional amounts for VAT related to our operations in Europe.

Our European operations are subject to the VAT which is usually applied to all goods and services purchased and sold throughout Europe. The VAT receivable was $4.4 million and $4.7 million as of December 31, 2016 and December 31, 2015, respectively. On April 14, 2009, December 21, 2009 and June 25, 2010, the ITA issued notices of assessment to 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, respectively. 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. Furth