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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2015

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 001-36620

Tokai Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-1000967**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
255 State Street, 6th Floor Boston, Massachusetts	**02109**
(Address of principal executive offices)	**(Zip code)**

(617) 225-4305
(Registrant's telephone number, including area code)

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

Title of Class	**Name of Exchange on Which Registered**
Common Stock, $0.001 par value	**NASDAQ Global Market**

Securities registered pursuant to Section 12(g) of the Act:
None.

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

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 ☑

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 ☑ 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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, 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 ☑
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 Exchange Act). Yes ☐ No ☑

As of June 30, 2015, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates was $128,484,663, based on the last reported sale price of such stock on the NASDAQ Global Market as of such date.

As of February 29, 2016, the registrant had 22,625,159 shares of Common Stock, $0.001 par value per share, outstanding.

Portions of the registrant's definitive proxy statement for its 2016 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end December 31, 2015, are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K.

TOKAI PHARMACEUTICALS, INC.
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Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the anticipated timing, cost and conduct of our pivotal Phase 3 clinical trial of galeterone and our efforts to complete the clinical development of galeterone for patients with AR-V7 positive metastatic castration resistant prostate cancer, or mCRPC;
- the anticipated timing, cost and conduct of additional clinical trials of galeterone;
- the development of a companion diagnostic test expected to be used commercially with galeterone;
- the timing and outcome of regulatory review of galeterone for the treatment of AR-V7 positive mCRPC;
- the development of galeterone for the treatment of prostate cancer or other indications or patient populations, and of any other future product candidates, including compounds that are designed to disrupt androgen receptor signaling through enhanced androgen receptor degradation;
- our plans to enter into collaborations for the commercialization of galeterone and any other future product candidates;
- the potential benefits of any future collaboration;
- the rate and degree of market acceptance and clinical utility of our products;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional products or product candidates with significant commercial potential;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I

ITEM 1. *BUSINESS*

Overview

We are a biopharmaceutical company focused on developing and commercializing innovative therapies for prostate cancer and other hormonally-driven diseases. Our lead drug candidate, galeterone, is an oral small molecule that utilizes the mechanistic pathways of current second-generation androgen signaling inhibitors, while also introducing a distinct third mechanism – androgen receptor degradation. We are developing galeterone for the treatment of patients with metastatic castration-resistant prostate cancer, or mCRPC.

We are conducting a pivotal Phase 3 clinical trial comparing galeterone to Xtandi® (enzalutamide) in approximately 148 treatment-naïve mCRPC patients whose prostate tumors express the AR-V7 splice variant. We refer to this clinical trial as ARMOR3-SV. We believe that the AR-V7 splice variant is the most common form of C-terminal loss, or the loss of the portion of the androgen receptor that contains the ligand-binding domain. C-terminal loss generally, and AR-V7 specifically, has been associated with poor responsiveness to commonly-used oral therapies for mCRPC. ARMOR3-SV is, to our knowledge, the first precision-medicine based pivotal clinical trial in prostate cancer. Selection of patients with AR-V7 is made using a clinical trial assay developed by our collaborator, Qiagen Manchester Limited, or Qiagen. We believe that the design of ARMOR3-SV is aligned with feedback that we obtained from the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA. We expect to complete enrollment in ARMOR3-SV by the end of 2016 and to have top-line data available from the study by mid-2017. We have been given fast track designation by the FDA for galeterone for the treatment of mCRPC.

As of December 31, 2015, galeterone had been administered to over 250 prostate cancer patients and healthy volunteers in clinical trials. In these trials, which included patients whose tumor cells did not express AR-V7, galeterone was well tolerated and clinically meaningful reductions in levels of prostate specific antigen, or PSA, a biochemical marker used to evaluate prostate cancer patients for signs of response to therapy, were observed in prostate cancer patients. Therefore, and subject to the availability of resources, we anticipate expanding the clinical development of galeterone in other indications or patient populations in prostate cancer.

We initially plan to conduct two additional open-label studies of galeterone in mCRPC patients who have shown resistance following treatment with either Xtandi or Zytiga® (abiraterone acetate). The first of these studies, which we anticipate initiating in the first half of 2016, is an expansion of an arm of our ongoing Phase 2 clinical trial of galeterone, referred to as ARMOR2, in mCRPC patients who have developed acquired resistance to Xtandi. The other study, which we also expect to initiate in the first half of 2016, is designed to evaluate galeterone in men whose mCRPC rapidly progressed after initial treatment with either Xtandi or Zytiga. We plan to evaluate all patients enrolled in this new Phase 2 clinical trial for the presence of AR-V7, but AR-V7 positive status is not a criterion for participation in this trial.

We have worldwide development and commercialization rights to galeterone. To maximize the value of these rights, we intend to build a urology- and oncology-focused specialty sales and marketing organization in the United States to support the commercialization of galeterone. We intend to commercialize galeterone outside the United States through collaborations with third parties.

Our Strategy

Our goal is to become a leading biopharmaceutical company that develops and commercializes innovative therapies for the treatment of prostate cancer and other hormonally-driven diseases. Our strategy includes the following components:

- ***Complete the clinical development of and seek marketing approval for galeterone for the treatment of AR-V7 positive mCRPC.*** ARMOR3-SV is designed to evaluate whether administration of galeterone

results in a statistically significant increase in radiographic progression free survival as compared to Xtandi in approximately 148 treatment-naive mCRPC patients whose prostate tumor cells express the AR-V7 splice variant. We expect ARMOR3-SV to be fully enrolled by the end of 2016, and to have top-line data from the trial by mid-2017.

- ***Develop galeterone for other prostate cancer indications and patient populations.*** Although we are currently focusing our initial development of galeterone on the treatment of AR-V7 positive mCRPC patients, we intend to evaluate galeterone in additional mCRPC patient populations. To this end, we plan to expand an arm of ARMOR2 in mCRPC patients who have developed acquired resistance to Xtandi. We also expect to initiate a new Phase 2 clinical trial designed to evaluate galeterone in men whose mCRPC rapidly progressed after initial treatment with either Xtandi or Zytiga.
- ***Maximize the commercial potential of galeterone.*** We have worldwide development and commercialization rights to galeterone. If galeterone is approved in the United States, we intend to build a urology- and oncology-focused specialty sales organization in the United States to support the commercialization of galeterone. We intend to commercialize galeterone outside the United States through collaborations with third parties.
- ***Advance the development of our second-generation androgen receptor degradation agents.*** We have a drug discovery program, known as ARDA (androgen receptor degradation agents), under which we are identifying and developing novel compounds designed to have potent androgen receptor degradation activity. Our most advanced series of compounds from this program are currently in preclinical development. We plan to target compounds developed under our ARDA program for patients with androgen receptor signaling diseases, including prostate cancer, either alone or in combination with other products.

The Treatment of Prostate Cancer

Prostate Cancer Overview

According to the American Cancer Society, in the United States, prostate cancer is the most frequently diagnosed cancer among men other than skin cancer. The American Cancer Society estimates that, in the United States, approximately 215,000 new cases of prostate cancer are diagnosed annually, and approximately 28,000 men will die from the disease each year. Overall, in the United States, about one in seven men will be diagnosed with prostate cancer during his lifetime, and about one in 36 men will die from the disease.

Prostate cancer is most frequently diagnosed at an early stage, when it is confined to the prostate gland and its immediate surroundings. Advances in screening and diagnosis, including the widespread use of PSA screening, have allowed detection of the disease in its early stages in approximately 85% of all cases diagnosed in the United States. Patients with early-stage disease are typically treated with surgery or radiation therapy, or in limited circumstances, with both. For the majority of men, these procedures are successful in curing the disease. However, for others, these procedures are not curative and their prostate cancer ultimately recurs. Men with recurrent prostate cancer are considered to have advanced prostate cancer. In addition, about 15% of men diagnosed with prostate cancer have metastatic disease at the time of diagnosis. Men with metastatic disease are also considered to have advanced prostate cancer. Men with advanced prostate cancer are most often treated with drug therapy.

Treatment of Advanced Prostate Cancer

The growth and survival of prostate cancer tumor cells depend primarily on the functioning of the androgen receptor signaling pathway. The pathway is ordinarily activated by the binding of androgens, such as testosterone and dihydrotestosterone, or DHT, to the ligand binding domain of androgen receptors in prostate cancer cells. Testosterone is primarily produced in the testes, adrenal glands and, to a lesser extent, in prostate cancer tumor cells. DHT is a product of enzymatic conversion of testosterone. Once binding has occurred, the bound androgen/

androgen receptor complex passes into the nucleus of the tumor cell where it binds to DNA in the cancer cell, triggering abnormal cell growth and tumor progression.

Because testosterone fuels prostate cancer growth, first-line therapy for advanced prostate cancer typically entails androgen deprivation therapy, or ADT, with luteinizing hormone releasing hormone, or LHRH, analogs such as the drug Lupron® (leuprolide). ADT reduces testosterone to levels that are commensurate with the levels of a male who has had surgical castration to minimize the testosterone that would otherwise fuel prostate cancer growth. Early-stage patients who receive and respond to this treatment are considered to have hormone-sensitive prostate cancer. ADT has been the principal option for the initial treatment of advanced prostate cancer for more than 50 years.

Most advanced prostate cancer patients initially respond to ADT. However, after initiation of ADT, almost all advanced prostate cancer patients experience a recurrence in tumor growth despite the reduction of testosterone to castrate levels. These patients are considered to be "castration resistant," and cancer that has reached this state is considered to be castration-resistant prostate cancer, or CRPC. The development of CRPC following initiation of ADT is due in part to tumor cells that have adapted to the hormone-deprived environment of the prostate and is generally diagnosed based on either rising levels of PSA or disease progression as evidenced by imaging tests or clinical symptoms. Patients treated with LHRH analogs typically remain on those drugs for the remainder of their lives in order to maintain castrate levels of testosterone.

During the course of ADT or following diagnosis of CRPC, most patients are treated with anti-androgens, which block the binding of androgens to the androgen receptor. An example of an anti-androgen marketed in the United States is the drug Casodex® (bicalutamide). Like LHRH analogs, the anti-androgens suppress tumor growth for a period of time in many CRPC patients. However, almost all CRPC patients develop resistance to anti-androgen therapy. Unlike LHRH analogs, however, patients do not typically remain on these drugs because these drugs have been shown to cause tumor growth once the cancer becomes resistant to the treatment. We refer to initial hormonal treatments like LHRH analogs and Casodex as primary hormonal treatments.

Patients with CRPC may have metastatic or non-metastatic disease. Metastatic cancer is cancer that has spread from the organ of origin to one or more locations in the body. Approximately 90% of mCRPC patients will develop metastases in the bone, which can cause pain, bone fracture, decreased quality of life and death. Approximately 30% of patients will develop metastases to solid organs, which can cause pain, decreased quality of life and potentially death. Metastases in the organs are referred to as visceral metastases. The liver and the lungs are the most common sites of visceral metastases.

Prior to 2010, the next line of treatment for patients who became resistant to primary hormonal treatment with LHRH analogs and anti-androgens was chemotherapy. At that time, the chemotherapy drug Taxotere® (docetaxel) was the primary FDA-approved treatment used for CRPC patients who were resistant to primary hormonal treatments, and there were no effective FDA-approved treatments for CRPC patients following chemotherapy. Since 2010, the FDA has approved five new agents for the treatment of patients with CRPC. These new treatments have provided patients with alternatives to chemotherapy and have resulted in differentiation of disease stages and new patient populations for which treatments can be developed.

Of these new agents, the two with the highest worldwide sales in 2015 were Zytiga and Xtandi. Zytiga was reported to have worldwide 2015 sales of $2.2 billion, and Xtandi was reported to have worldwide 2015 sales of $1.9 billion. Zytiga and Xtandi are members of a class of new drugs that act by disrupting the androgen receptor signaling pathway. We refer to this class of drugs as secondary hormonal treatments.

Zytiga is an oral secondary hormonal treatment approved by the FDA in April 2011 for use in combination with prednisone to treat men with post-chemotherapy mCRPC. In December 2012, the FDA expanded the approval of Zytiga in combination with prednisone to include treatment of pre-chemotherapy mCRPC patients.

Zytiga disrupts the androgen receptor signaling pathway by inhibiting CYP17 and reducing production of testosterone in the testes, adrenal glands and prostate cancer tumor cells.

Xtandi is an oral secondary hormonal treatment approved by the FDA in August 2012 to treat men with post-chemotherapy mCRPC. In September 2014, the FDA expanded the approval of Xtandi to include treatment of pre-chemotherapy mCRPC patients. Xtandi is an androgen receptor antagonist that disrupts the androgen receptor signaling pathway by blocking the binding of testosterone or the androgen DHT with the androgen receptor.

Other new agents include Jevtana® (cabazitaxel), a chemotherapeutic agent for use in combination with prednisone to treat men with mCRPC following first-line chemotherapy, Provenge® (sipuleucel-T), a prostate cancer immunotherapy to treat men with asymptomatic or minimally symptomatic mCRPC, whether pre-chemotherapy or post-chemotherapy, and Xofigo® (radium-223), a bone targeting radiopharmaceutical for the treatment of CRPC patients with symptomatic bone metastases and no visceral metastases that are detectable upon imaging.

Prior to the approval of the new agents, patients had no effective treatment alternatives following chemotherapy. Each of the new agents, however, has been approved for use following chemotherapy. Patients who have undergone chemotherapy treatment and treatment with Zytiga or Xtandi and whose disease has progressed are referred to as salvage patients. There are only limited treatment options for salvage patients.

The treatment of patients with advanced prostate cancer varies depending on the status of the disease, including whether it is metastatic, and depending on the prior treatments that patients have undergone. Figure 1 below identifies the various patient populations within advanced prostate cancer and the treatments that are approved by the FDA for these populations.

Figure 1: Summary of FDA Approved Treatments for Advanced Prostate Cancer Populations

Patient Populations / Treatment Options		Non-Metastatic		Metastatic			
				CRPC			
		Hormone-Sensitive	CRPC	Pre-Chemo	First-Line Chemo	First-Line Post-Chemo	Salvage
Primary Hormonal Treatment	LHRH	✓	✓	✓	✓	✓	✓
	Androgen Receptor Antagonists	✓	✓				
Secondary Hormonal Treatment	Zytiga			✓		✓	
	Xtandi			✓		✓	
Chemotherapy	Taxotere				✓		
	Jevtana					✓	✓
Immunotherapy	Provenge			✓		✓	
Bone Targeting Agent	Xofigo			✓	✓	✓	✓

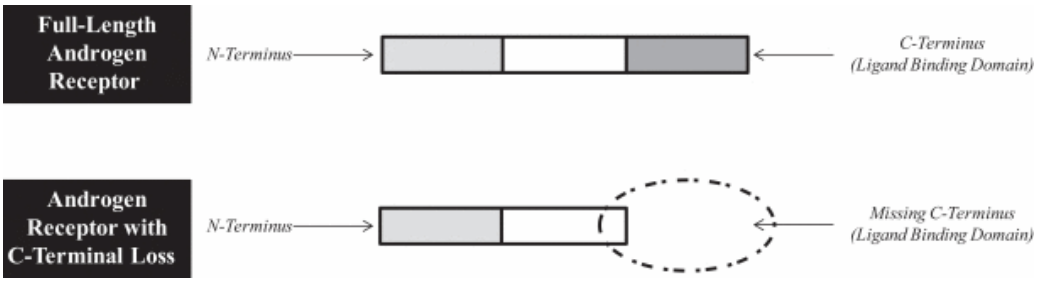
We are aware of a number of additional therapies that are in late stage clinical trials for prostate cancer, including additional secondary hormonal treatment candidates that are designed to act by the same mechanisms of action of Zytiga and Xtandi.

Despite the new therapies, including Zytiga and Xtandi and the additional drug candidates in late-stage clinical development, we believe that there continues to be an unmet need as there are patient populations that may not be effectively addressed by these therapies, such as mCRPC patients with C-terminal loss. Zytiga and Xtandi also have treatment limitations, including efficacy limitations, risk of resistance, risks associated with the co-administration of prednisone with Zytiga, a potential seizure risk observed with Xtandi and a complicated dosing regimen for Zytiga.

Unmet Need in Prostate Cancer Patients with C-Terminal Loss

The growth and survival of prostate cancer tumor cells depend primarily on the functioning of the androgen receptor signaling pathway. The pathway and tumor cell growth is ordinarily activated by the binding of androgens, such as testosterone and DHT, to the ligand binding domain of androgen receptors in prostate cancer cells. All proteins, including androgen receptors, are made up of a chain of amino acids that has an N-terminus at one end of the chain and a C-terminus at the other end of the chain as shown in the full-length androgen receptor depicted in Figure 2 below. In the case of androgen receptors, the C-terminus contains the ligand binding domain. The effectiveness of therapies like Zytiga and Xtandi, which act solely through CYP17 inhibition or androgen receptor antagonism, requires a functional ligand binding domain. As depicted in Figure 2 below, in the case of prostate tumor cells that express truncated androgen receptors with C-terminal loss, there is no functional ligand binding domain. This lack of a functional ligand binding domain causes the truncated androgen receptor to be constitutively active, or continuously signaling, meaning that activation of the androgen receptor pathway and tumor growth occurs even in the absence of androgens and androgen binding. As a result, we believe that patients with truncated androgen receptors with C-terminal loss may not be effectively treated by these therapies.

Figure 2: Full-Length Androgen Receptor and Androgen Receptor with C-Terminal Loss



These limitations of CYP17 inhibitors and androgen receptor antagonists have been supported by investigator-initiated studies conducted at several leading academic medical centers in which the presence of C-terminal loss or AR-V7 in patients was associated with poor responsiveness of patients' prostate tumors to Zytiga and Xtandi. Published data, however, have shown activity of docetaxel, a chemotherapeutic agent, in AR-V7 positive mCRPC patients.

MD Anderson. At The American Society of Clinical Oncology, or ASCO, 2014 Annual Meeting, researchers from MD Anderson presented data from a clinical study in which 60 mCRPC patients with bone metastases were treated with a sequential combination regimen of Zytiga and Xtandi. In the study, the researchers defined primary resistance as discontinuation of therapy due to symptomatic or imaging evidence of disease progression within four months of initiating treatment and benefit as discontinuation of therapy due to symptomatic or imaging evidence of disease progression at least four months after initiating treatment. In a subset of 15 patients who were evaluable for C-terminal loss, four patients were identified as having C-terminal loss, including two who were identified as having AR-V7. In this study, the researchers used antibody-based assays to identify the presence of C-terminal loss and AR-V7. All four, or 100%, of these patients showed

primary resistance. Of the 11 patients in the subset that did not have C-terminal loss or AR-V7, nine patients, or 82%, showed benefit. These data are set forth in Table 1 below.

Table 1: Summary of MD Anderson C-Terminal Loss and AR-V7 Findings (*ASCO 2014*)

	N	Primary Resistance	Benefit
AR-V7 positive	2	100%(2/2)	0%(0/2)
C-terminal loss (excluding AR-V7)	2	100%(2/2)	0%(0/2)
Negative for AR-V7 and C-terminal loss	11	18%(2/11)	82%(9/11)

In addition, researchers from MD Anderson presented the results of a second study in an article published in *European Urology* in May 2014. In the study, the researchers evaluated bone biopsy specimens from CRPC patients with bone metastases that had been treated with Xtandi to evaluate the effects of Xtandi on cancer and to associate these effects with clinical observations. In the study, the researchers defined resistance and benefit as follows:

- primary resistance, as discontinuation of therapy due to symptomatic or imaging evidence of disease progression within four months of initiating Xtandi treatment;
- moderate benefit, as discontinuation of therapy due to symptomatic or imaging evidence of disease progression within four to six months of initiating Xtandi treatment; and
- prolonged benefit, as discontinuation of therapy due to symptomatic or imaging evidence of disease progression at least six months after initiating Xtandi treatment.

The researchers evaluated a population of 23 patients who had two evaluable biopsies for AR-V7. As shown in Table 2 below, based on identification of AR-V7 at baseline, 86% of the patients with AR-V7 showed primary resistance, and 38% of the patients that did not have AR-V7 showed primary resistance.

Table 2: Summary of MD Anderson AR-V7 Baseline *(European Urology)*

Outcome	N	Primary Resistance	Moderate Benefit	Prolonged Benefit
AR-V7 positive	7	86%(6/7)	14%(1/7)	0%(0/7)
AR-V7 negative	16	38%(6/16)	31%(5/16)	31%(5/16)

Johns Hopkins. In a clinical trial conducted by Johns Hopkins and published in the *New England Journal of Medicine* in September 2014, researchers prospectively evaluated the effect of AR-V7 in patients with mCRPC on tumor responsiveness to treatment with Xtandi and Zytiga. In the trial, 31 patients received Xtandi, and 31 patients received Zytiga. In the trial, the presence of AR-V7 was determined by an analysis of circulating tumor cells, or CTCs, isolated from the patient's blood. In the Xtandi-treated group, 12 of the 31 patients were identified as having AR-V7. None of these 12 patients with AR-V7 achieved the trial's primary endpoint of maximal PSA reduction of at least 50%. Eleven of the 12 patients with AR-V7 did not achieve any PSA reduction. Ten of the 19 patients who did not have AR-V7 achieved a maximal PSA reduction of at least 50%. In addition, the median radiographic progression free survival, or rPFS, and the median overall survival of the patients with AR-V7 was 2.1 months and 7.4 months, respectively, compared to 6.1 months and 16.0 months, respectively, in the patients without AR-V7. The differences between the AR-V7 and non-AR-V7 groups in terms of the number of patients achieving a maximal PSA reduction of 50% and the improvements in median rPFS and overall survival were statistically significant.

In the Zytiga-treated group, six of the 31 patients were identified as having AR-V7. None of the six patients with AR-V7 achieved any PSA reduction during treatment. Seventeen of the 25 patients who did not have AR-V7 achieved a maximal PSA reduction of at least 50%. The median rPFS and the median overall survival of

the patients with AR-V7 was 2.3 months and 11.1 months, respectively, and in each case had not been reached in the patients without AR-V7. The differences between the AR-V7 and non-AR-V7 groups in terms of the number of patients achieving a maximal PSA reduction of 50% and the improvements in median rPFS and overall survival were statistically significant. The data from the Johns Hopkins trial are summarized in Table 3 below.

Table 3: Summary of Johns Hopkins Data (*New England Journal of Medicine*)

				Results					
Treatment	*N*	*AR-V7+*	*AR-V7 Status*	*PSA50*	*P-value**	*rPFS*	*P-value**	*Overall survival*	*P-value**
Xtandi	31	38% (12/31)	+	0%	0.004	2.1 months	<0.001	7.4 months	<0.001
			-	52%		6.1 months		16.0 months	
Zytiga	31	19%(6/31)	+	0%	0.004	2.3 months	<0.001	11.1 months	<0.001
			-	68%		Not Reached		Not Reached	

* Results are considered statistically significant if they have a P-value of less than 0.05, meaning that there is less than a one-in-20 likelihood that the observed results occurred by chance.

The Johns Hopkins researchers also reported the prevalence of AR-V7 in different patient groups participating in the trial based on the prior treatment the patient had received. Table 4 below sets out the percentage of patients in each prior treatment group who had AR-V7 as detected in CTCs.

Table 4: Prevalence of AR-V7 in CRPC in the Johns Hopkins Trial (*New England Journal of Medicine*)

Treatment Status Prior to Entry Into Johns Hopkins Trial	Percentage of Patients in Pre-Treatment Group who had AR-V7 in CTCs
Pre-enzalutamide *and* pre-abiraterone acetate	11.6%
Post-enzalutamide *only*	25.0%
Post-abiraterone acetate *only*	51.2%
Post-enzalutamide *and* post-abiraterone acetate	66.7%

Based on these data, we believe that treatment with Xtandi and Zytiga may be associated with an increase in the prevalence of AR-V7 and cross-resistance to sequential therapy, thereby leaving patients who are treated with either Xtandi or Zytiga with no currently available secondary hormonal treatment options. By contrast, we believe galeterone has the potential to reduce the prevalence of AR-V7 through its mechanism of androgen receptor degradation.

Memorial Sloan Kettering. At the European Society for Clinical Oncology 2014 Congress, researchers from Memorial Sloan Kettering presented data from a clinical study in which 85 mCRPC patients were treated with Xtandi, Zytiga or taxane-based chemotherapy. Of the 46 patients who received either Xtandi or Zytiga, 21 showed no reduction in PSA levels and were considered resistant to therapy and 25 showed a reduction in PSA levels and were considered to have had a clinical benefit. All patients were screened at baseline for C-terminal loss. A retrospective analysis was conducted in which patients with C-terminal loss were assessed as having demonstrated primary resistance or clinical benefit. Of the six patients identified as having C-terminal loss, no patient showed a clinical benefit. Sixty-three percent of the patients who did not have C-terminal loss showed clinical benefit. These data are summarized in Table 5 below.

Table 5: Summary of Memorial Sloan Kettering C-Terminal Loss Findings

	N	Primary Resistance	Benefit
C-terminal loss	6	100% (6/6)	0% (0/6)
Negative for C-terminal loss	40	37% (15/40)	63% (25/40)

Vancouver Prostate Centre. At the ASCO Genitourinary Cancers Symposium held in January 2016, researchers from the Vancouver Prostate Centre and the University of British Columbia presented data from a clinical study conducted in 37 mCRPC patients who had not received either Xtandi or Zytiga. In the trial, the presence of AR-V7 was determined using a whole blood assay that did not require analysis of CTCs. Four of the 37 patients, or 11%, were identified as being AR-V7 positive. Zytiga was administered to all 37 patients enrolled in the study. None of the AR-V7 positive patients achieved a maximal PSA reduction of at least 50%, while 42% of the AR-V7 negative patients achieved a maximal PSA reduction of at least 50%. The median progression-free survival and the median overall survival of the patients with AR-V7 were 0.7 months and 6.6 months, respectively, as compared to 4.0 months and 22.1 months in the AR-V7 negative patients. The data from the Vancouver trial are summarized in Table 6 below.

Table 6: Summary of Vancouver Data

Treatment	*N*	*AR-V7+*	*AR-V7 Status*	*PSA50*	*Progression-free survival*	*Overall survival*
Zytiga	37	11% (4/37)	+	0%	0.7	6.6
			-	42%	4.0	22.1

Galeterone

Overview

Our lead product candidate, galeterone, is an oral small molecule that utilizes the mechanistic pathways of current second-generation androgen signaling inhibitors, while also introducing a distinct mechanism – androgen receptor degradation. We are developing galeterone for the treatment of patients with mCRPC.

We are conducting ARMOR3-SV, a pivotal Phase 3 clinical trial comparing galeterone to Xtandi in approximately 148 treatment-naive mCRPC patients whose prostate tumors express the AR-V7 splice variant. We believe that the AR-V7 splice variant is the most common form of C-terminal loss, or the loss of the portion of the androgen receptor that contains the ligand-binding domain. C-terminal loss generally, and AR-V7 specifically, has been associated with poor responsiveness to commonly-used oral therapies for mCRPC. ARMOR3-SV is, to our knowledge, the first precision-medicine based pivotal clinical trial in prostate cancer. Selection of patients with AR-V7 is made using a clinical trial assay developed by our collaborator, Qiagen. We believe that the design of ARMOR3-SV is aligned with feedback that we obtained from the FDA and the EMA. We expect to complete enrollment in ARMOR3-SV by the end of 2016 and to have top-line data available from the study by mid-2017. We have been given fast track designation by the FDA for galeterone for the treatment of mCRPC.

As of December 31, 2015, galeterone had been administered to over 250 prostate cancer patients and healthy volunteers in clinical trials. In these trials, which included patients whose tumor cells did not express AR-V7, galeterone was well tolerated and clinically meaningful reductions in PSA levels were observed in prostate cancer patients. Therefore, and subject to the availability of resources, we anticipate expanding the clinical development of galeterone in other indications or patient populations in prostate cancer.

We initially plan to conduct two additional open-label studies of galeterone in mCRPC patients who have shown resistance following treatment with either Xtandi or Zytiga. The first of these studies, which we anticipate initiating in the first half of 2016, is an expansion of an arm of our ARMOR2 trial in mCRPC patients who have developed acquired resistance to Xtandi. The other study, which we also expect to initiate in the first half of 2016, is designed to evaluate galeterone in men whose mCRPC rapidly progressed after initial treatment with either Xtandi or Zytiga. We plan to evaluate all patients enrolled in this new Phase 2 clinical trial for the presence of AR-V7, but AR-V7 positive status is not a criterion for participation in this trial.

We have worldwide development and commercialization rights to galeterone. To maximize the value of these rights, we intend to build a urology- and oncology-focused specialty sales and marketing organization in the United States to support the commercialization of galeterone. We intend to commercialize galeterone outside the United States through collaborations with third parties.

Key Differentiating Attributes of Galeterone

Based on preclinical and clinical data, we believe that galeterone has advantages over Zytiga and Xtandi because of the following key differentiating attributes:

- ***Potential for improved efficacy.*** We believe that galeterone, which combines the mechanism of action of androgen receptor degradation with the mechanisms of action of Zytiga (CYP17 inhibition) and Xtandi (androgen receptor antagonism), may further improve progression-free survival and overall survival beyond that of products that depend on only a single mechanism of action. In 2014, we reported efficacy data from a total of 107 CRPC patients in our ARMOR2 trial that showed clinically meaningful reductions in maximal PSA in patients in the trial.
- ***Potential for efficacy in CRPC patients with C-terminal loss, including AR-V7.*** Because galeterone's distinct mechanism of action of androgen receptor degradation does not require an intact ligand binding domain to be effective against prostate cancer tumors, we believe galeterone may be effective in prostate cancer tumors that express altered androgen receptors with C-terminal loss, including AR-V7. In contrast, the mechanisms of action of Zytiga and Xtandi and other similar drugs in clinical development all require the presence of the ligand binding domain in order to be effective.
- ***Potential for lower risk of resistance.*** We believe that galeterone may reduce the risk of or delay the development of resistance to therapy because galeterone addresses multiple mechanisms of action simultaneously. We believe that reducing resistance may delay the development of disease progression.
- ***Potential for broad utility in prostate cancer.*** We believe that galeterone may be well suited to treat different prostate cancer patient populations, from early-stage prostate cancer patients to end-stage salvage mCRPC patients, because of its efficacy, safety and tolerability.
- ***Favorable safety profile.*** As of December 31, 2015, we had administered galeterone to over 250 prostate cancer patients and healthy volunteers in Phase 1 and Phase 2 clinical trials. In these trials, galeterone demonstrated a favorable safety and tolerability profile. In our ARMOR2 trial, approximately 90% of all treatment-emergent related adverse events reported as of December 31, 2015 were grade 1 or 2 in severity and were generally manageable and reversible.
- ***No requirements for steroids.*** Unlike Zytiga, galeterone has not been shown in clinical trials to cause mineralocorticoid excess and does not require co-administration of steroids. Because Zytiga has been shown in clinical trials to cause mineralocorticoid excess, a potentially fatal syndrome characterized by hypertension, hypokalemia, fluid retention and edema, Zytiga is required to be administered with prednisone to reduce the frequency of patients exhibiting mineralocorticoid excess. Despite the co-administration of prednisone, however, approximately 30% of patients treated with Zytiga in a pivotal Phase 3 trial developed symptoms of mineralocorticoid excess. In addition, the chronic use of prednisone poses other safety concerns. Side effects associated with chronic use of prednisone include muscle weakness, osteoporosis, diabetes and increased risk of infection.
- ***No associated seizure risk.*** Unlike Xtandi, we have not had any reports of seizures in clinical trials of galeterone. A 0.9% risk of grand mal seizures was reported in the Xtandi pivotal Phase 3 trial in post-chemotherapy CRPC patients. These seizures have been linked to the inhibition or antagonism by Xtandi of $GABA_A$, a receptor associated with the nervous system. Galeterone is not a $GABA_A$ antagonist.
- ***Ease of dosing.*** Unlike the complicated dosing regimen for Zytiga, galeterone is dosed orally once per day and does not require the co-administration of steroids. We believe that this convenient dosing

regimen will enhance patient compliance. In contrast, Zytiga must be taken in a fasted state to avoid large increases in absorption, which may cause side effects. Zytiga also must be co-administered with steroids. Prednisone, the steroid co-administered with Zytiga, must be taken with food in order to avoid potential development of gastric ulcers. As a result, Zytiga and prednisone cannot be taken together and dosing must be carefully coordinated with food intake, resulting in a staggered dosing regimen of pills three times per day.

Galeterone Clinical Development

We refer to our clinical development program for galeterone as the Androgen Receptor Modulation Optimized for Response, or ARMOR, program. We submitted an investigational new drug application, or IND, to the FDA for galeterone for the treatment of CRPC in August 2009 and began clinical trials of galeterone in November 2009. As of December 31, 2015, we had enrolled 121 CRPC patients in our ongoing ARMOR2 trial and 49 CRPC patients in our Phase 1 ARMOR1 trial, which used a prior formulation of galeterone. In four additional Phase 1 clinical trials, we also administered galeterone to 102 healthy volunteers. We are currently enrolling patients in ARMOR3-SV, our pivotal Phase 3 clinical trial of galeterone.

ARMOR2

In December 2012, we initiated our ARMOR2 trial, an open label Phase 2 clinical trial of galeterone. The trial was designed as a two-part trial. Part 1 of the trial was a dose escalation phase designed to confirm the dose of galeterone to be evaluated in Part 2 of the trial. Part 2 of the trial was designed to evaluate the efficacy and safety of galeterone at the dose selected in Part 1 in distinct CRPC patient populations. Enrollment in the trial has been completed. As of December 31, 2015, 11 patients were still participating in the trial.

The primary efficacy endpoints of our ARMOR2 trial are based on a decrease in PSA levels. In setting the primary endpoints of the trial, we considered the standard, accepted use of monitoring PSA levels to determine if a patient's prostate cancer is responding to therapy as well as the use of reductions in PSA levels as a key efficacy endpoint in Phase 2 clinical trials of other prostate cancer agents, as set forth in guidelines developed by the Prostate Cancer Working Group 2, or PCWG2. PCWG2 is an international group of prostate cancer investigators who published guidelines for the design and evaluation of prostate cancer trials.

Part 1 of ARMOR2 Trial. In Part 1 of the trial, we enrolled 25 CRPC treatment-naïve patients with progressive disease and three patients whose disease progressed during treatment with Zytiga, whom we refer to as Zytiga-refractory patients. The CRPC treatment-naïve patients were enrolled in one of three escalating dose cohorts: six patients at 1700 mg/day, 11 patients at 2550 mg/day and eight patients at 3400 mg/day. The Zytiga-refractory patients all received doses of 2550 mg/day. All patients in Part 1 of the trial received treatment for up to an initial period of 12 weeks followed by optional continued dosing for those patients who tolerated treatment and did not show signs of disease progression. Treatment was continued until disease progression or patient withdrawal due to adverse events or other reasons.

At least 50% of patients at all dose levels achieved a 30% or greater decrease in PSA. Based on the recommendation of the monitoring committee for the trial following review of safety, efficacy and pharmacokinetic results of the three dose groups, we chose the 2550 mg/day dose for further study in Part 2 of the ARMOR2 trial.

Part 2 of ARMOR2 Trial. In Part 2 of ARMOR2, we initially enrolled 93 patients and are evaluating galeterone dosed at 2550 mg/day in the following CRPC populations:

- non-metastatic CRPC and mCRPC treatment-naïve patients;
- Zytiga-refractory patients; and
- patients whose disease progressed during treatment with Xtandi, whom we refer to as Xtandi-refractory patients.

The primary endpoints for Part 2 of ARMOR2 were as follows:

- Treatment-naïve patients: percentage of patients having a maximal reduction in PSA levels of at least 30% from baseline to the end of the primary treatment phase; and
- Zytiga-refractory and Xtandi-refractory patients: percentage of change in PSA levels from baseline to the end of the primary treatment phase.

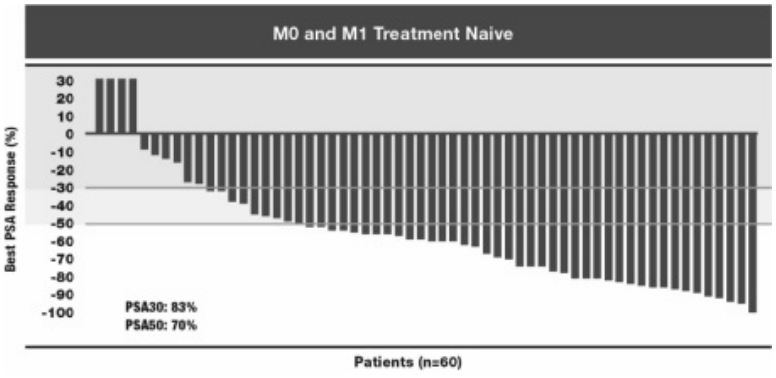
Additional endpoints include incidence of adverse events, change from baseline in safety parameters, response rate, and CTC enumeration and characterization, including for the evaluation of C-terminal androgen receptor expression in relation to N-terminal androgen receptor expression to identify C-terminal loss and the lack of a functional ligand binding domain.

Patients enrolled in Part 2 of the trial were to receive treatment with galeterone at a dose of 2550 mg/day for an initial period of up to 12 weeks, followed by optional continued dosing in an extension phase for those patients who tolerated treatment and did not show signs of disease progression. Treatment is continued until disease progression or patient withdrawal due to adverse events or other reasons. Enrollment of these 93 patients was completed in July 2014 and, as of December 31, 2015, 11 patients remained on study in the extension phase.

We recently re-opened the arm of ARMOR2 evaluating Xtandi-refractory patients to enroll up to 21 additional patients. See "—Galeterone Development Program– Other Development Activities" below.

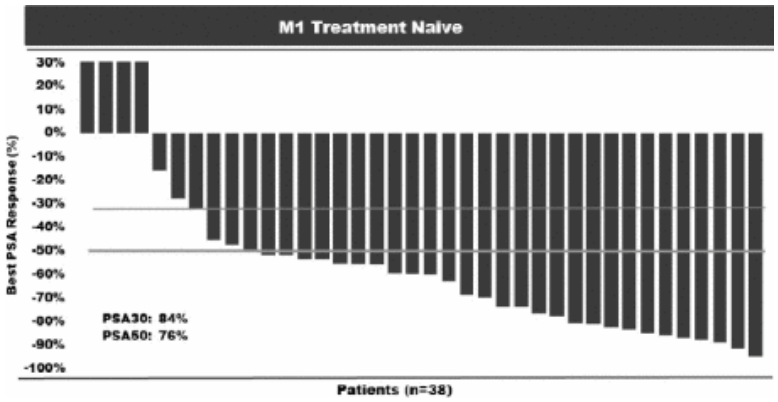
Phase 2 Data Presentation. In November 2014, we presented interim efficacy and safety data from our ARMOR2 trial for patients who received the 2550 mg/day dose of galeterone at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, or EORTC. In 60 evaluable treatment-naïve CRPC patients in Part 1 and Part 2 of the trial who received the 2550 mg/day dose of galeterone, during the first 12 weeks of dosing, 83% had a maximal reduction in PSA levels of at least 30%, and 70% had a maximal reduction in PSA levels of at least 50%, as described in Figure 3 below.

Figure 3: ARMOR2: 12-Week Maximal PSA Response Waterfall Plot in All Treatment-Naïve CRPC Patients (n=60) (2550 mg dose)



In 38 treatment-naïve mCRPC patients who received the 2550 mg/day dose, during the first 12 weeks of dosing, 84% had a maximal reduction in PSA levels of at least 30%, and 76% had a maximal reduction in PSA levels of at least 50%, as described in Figure 4 below.

Figure 4: ARMOR2: 12-Week Maximal PSA Response Waterfall Plot in Treatment-Naïve mCRPC Patients Treated (n=38) (2550 mg dose)

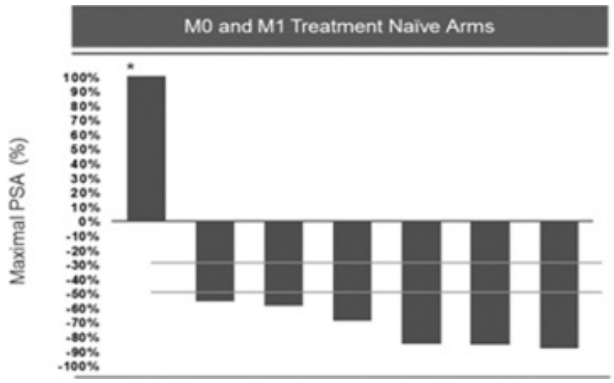


We also reported 12-week data for 37 Zytiga-refractory patients, 13 of whom showed a reduction in PSA levels, and nine Xtandi-refractory patients, five of whom showed a reduction in PSA levels.

Of the 16 treatment-naïve patients evaluable by Response Evaluation Criteria in Solid Tumors, or RECIST, three patients had a partial response and 11 patients had stable disease. Fifteen of the Zytiga-refractory patients and three of the Xtandi-refractory patients were evaluable by RECIST. Of these patients, five Zytiga-refractory patients had stable disease, and one Xtandi-refractory patient had stable disease. As measured by RECIST criteria, stable disease is achieved when the tumor has not increased in size by 20% and has not decreased by 30%, a partial response occurs when the tumor has decreased in size by at least 30%, and progressive disease occurs when the tumor has increased in size by at least 20% or new tumor lesions are identified.

Our ARMOR2 trial included CTC enumeration and characterization. At EORTC, we presented data from a retrospective subset analysis in which seven treatment-naïve CRPC patients in ARMOR2 were identified as having C-terminal loss as determined by the evaluation of C-terminal androgen receptor expression in relation to N-terminal androgen receptor expression. The assay used to evaluate C-terminal loss was the same one used in the study conducted at Memorial Sloan Kettering described above. As shown in Figure 5 below, six of these patients had maximal reductions in PSA levels of at least 50%. The seventh patient, who did not show any PSA reduction, discontinued therapy due to an adverse event unrelated to galeterone after approximately six weeks in the trial and did not receive the full treatment regimen. These data are supportive of galeterone's mechanism of action of androgen receptor degradation, which does not require a functional ligand binding domain.

Figure 5: ARMOR2: 12-Week Maximal PSA Response Waterfall Plot in All Treatment-Naïve CRPC with C-Terminal Loss (n=7) (2550 mg dose)



At EORTC, we also presented interim safety results from all 107 patients treated in the 2550 mg/day dose cohort as of October 14, 2014 in ARMOR2. In these patients, galeterone was well tolerated. Approximately 90% of all treatment-emergent related adverse events reported were grade 1 or 2 in severity and were generally manageable and reversible. The majority of these events were assessed as not related or unlikely related to galeterone. In addition, there were no reported cases of seizure or mineralocorticoid excess. The most common treatment-emergent related adverse events were nausea, fatigue, pruritus, decreased appetite, diarrhea, hypokalemia and vomiting.

As of December 31, 2015, nine of the 121 patients enrolled in ARMOR2 experienced a serious adverse event that was assessed by the investigator as related or possibly related to the administration of galeterone. No single treatment-related serious adverse event occurred in more than one patient. To date, no adverse events have resulted in interruptions or delays of our clinical trials.

ARMOR3-SV

We are currently enrolling patients in ARMOR3-SV, our pivotal Phase 3 clinical trial of galeterone. ARMOR3-SV trial is a randomized clinical trial comparing galeterone to Xtandi in approximately 148 treatment-naïve mCRPC patients whose prostate tumors express the AR-V7 splice variant. Under the trial protocol, patients are randomized on a one-to-one basis to receive either galeterone or the control arm treatment, Xtandi. Patients in the galeterone arm receive a dose of 2550 mg/day, and patients in the Xtandi arm receive a dose of 160 mg/day. All patients will continue to receive treatment until they have radiographic evidence of disease progression as determined by a blinded, independent central imaging assessment or patient withdrawal due to adverse events or other reasons. We have established an independent data monitoring committee for the trial. We believe the design of ARMOR3-SV is aligned with feedback that we obtained from the FDA and the EMA.

Only patients with the AR-V7 splice variant are being enrolled in the trial. These patients are identified by analysis of a blood sample at a central laboratory using an AR-V7 specific clinical trial assay developed under our collaboration with Qiagen. We expect that we may need to screen more than 1,500 patients to identify and enroll the target number of 148 patients with AR-V7.

The primary endpoint of the trial is rPFS as determined by a blinded, independent central imaging assessment measured from the time of patient randomization to the time of radiographic evidence of disease progression or time of death from any cause. In order to achieve the primary endpoint, results from the trial must demonstrate an 82% increase in median rPFS in the galeterone arm as compared to the Xtandi arm. Such a result

would be statistically significant and would likely be considered a clinically relevant outcome. The secondary endpoints include overall survival, safety, and time to next anti-cancer intervention or time to next cytotoxic therapy.

ARMOR3-SV is being conducted at over 100 clinical sites in several countries across North America, Western Europe and Australia. We expect to complete enrollment in the trial by the end of 2016 and to have top-line data from the trial by mid-2017. Our anticipated time to completion of enrollment and top-line data is subject to our continued ability to initiate clinical trial sites, our ability to recruit eligible patients, the prevalence of patients with the AR-V7 splice variant, the sensitivity of our clinical trial assay in detecting AR-V7 in patients, the satisfaction by AR-V7 positive patients of other eligibility criteria for participation in the trial, and disease progression of the patients enrolled in the trial. The rate of patient enrollment in the trial is difficult to predict as we have limited experience recruiting patients with AR-V7 for a clinical trial, and the percentage of mCRPC patients with AR-V7 is subject to widely varying projections in published literature. Moreover, because we have not previously conducted a clinical trial of galeterone in patients with AR-V7 or conducted a clinical trial using our AR-V7 clinical trial assay, and clinical trials of Xtandi in AR-V7 positive patients have only been conducted in a limited number of patients at single clinical sites, our assumptions concerning patient prevalence and rates of disease progression may be incorrect. In addition, a higher percentage of AR-V7 positive patients than we anticipate may elect not to participate in ARMOR3-SV or fail to meet the other eligibility criteria for participation in the trial. As a result, there can be no assurance that we will fully enroll, have top-line data from, or complete the trial when we anticipate.

Prospective Identification of AR-V7

We have entered into a collaboration with Qiagen to develop the clinical trial assay being used in ARMOR3-SV and to develop and commercialize a companion diagnostic test based on that assay for use with galeterone. Clinical data obtained with the clinical trial assay in the ARMOR3-SV trial will be used by Qiagen to support regulatory filings for the approval of the companion diagnostic for AR-V7 and by us to support our regulatory filings for approval of galeterone. We have also entered into an exclusive, worldwide license with Johns Hopkins to patent applications and know how covering certain assays to identify androgen receptor variants for use as a companion diagnostic with galeterone. One of these assays was used by Johns Hopkins in its prospectively designed clinical trial, reported in the *New England Journal of Medicine*, which assessed the impact of AR-V7 expression on patient responsiveness to Zytiga and Xtandi. We have discussed with the FDA our development strategy and plans for identifying AR-V7 patients in the ARMOR3-SV trial, including our plans to develop a companion diagnostic test based on our clinical trial assay. While we were not required to submit an investigational device exemption, or IDE, for the clinical trial assay to the FDA before we started screening patients in the ARMOR3-SV trial, we believe that the companion diagnostic test will need to be approved by the FDA through its Premarket Approval, or PMA, process. We anticipate that Qiagen will seek approval for the companion diagnostic test by the FDA in parallel with our seeking approval of galeterone in the United States.

We have also consulted with the EMA regarding our development strategy and plans for identifying AR-V7 patients in our ARMOR3-SV trial. Based on these consultations, we believe that the companion diagnostic test will need to be CE marked in connection with the submission for regulatory approval in the European Union. We have arranged with Qiagen to meet this requirement.

Under our agreement with Qiagen, Qiagen is responsible for developing, and obtaining and maintaining regulatory approvals for the AR-V7 companion diagnostic test in the United States, the European Union, Canada, Australia and such other countries as we and Qiagen may agree. In addition, Qiagen has agreed to use commercially reasonable and diligent efforts to manufacture the companion diagnostic test and to make the companion diagnostic test commercially available in those countries in which we have obtained regulatory approval for, and have valid patent claims covering, galeterone. Qiagen will be responsible for commercializing the companion diagnostic in each such country. If Qiagen elects not to commercialize the companion diagnostic test itself in any such country, for so long as there are valid patent claims covering galeterone in such country,

Qiagen has agreed to procure alternative distribution channels or otherwise supply the companion diagnostic test to us in order for us to market galeterone in combination with the companion diagnostic test. Upon our request, we and Qiagen have also agreed to negotiate in good faith to expand the scope of the projects under the agreement to, among other things, provide for the development and commercialization of the AR-V7 companion diagnostic test for use with galeterone in Japan.

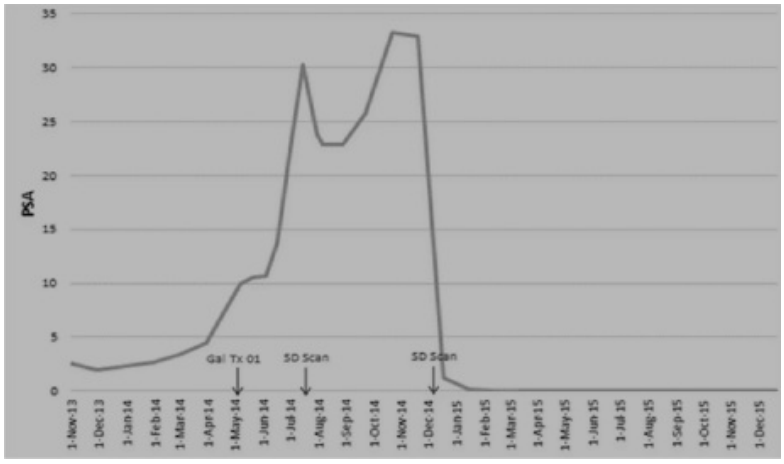
Subject to the terms of our agreement with Qiagen, we will pay Qiagen an approximate aggregate amount of up to $7.4 million over the term of the development program, including amounts paid to Qiagen for us to have the exclusive right to have CTC enrichment technology used in the development of the clinical trial assay. In addition, we have agreed to reimburse Qiagen for certain direct, out-of-pocket costs incurred by Qiagen, including for sample materials, which costs are estimated to equal in the aggregate up to $2.2 million. These amounts are subject to adjustment if we and Qiagen determine that changes in the scope of the development program are required. As of December 31, 2015, we have expensed an aggregate of $3.3 million in fees and $0.9 in out-of-pocket costs under our agreement with Qiagen. Following commercialization, we will have no further payment obligations to Qiagen under the agreement. We will not, however, receive any revenues from future sales, if any, of the AR-V7 companion diagnostic test.

The agreement with Qiagen expires on the later to occur of (i) the fifth anniversary of regulatory approval of the AR-V7 companion diagnostic test and (ii) the expiration of Qiagen's commercialization obligations under the agreement. We are permitted to terminate the agreement for convenience upon 180 days' written notice to Qiagen. Either party may terminate the agreement upon 60 days' written notice to the other party based on uncured material breaches by the other party and may terminate the agreement immediately based on the bankruptcy or insolvency of the other party.

Other Development Activities

Although we are currently focusing our initial development of galeterone on the treatment of AR-V7 positive mCRPC patients, we intend to evaluate galeterone in additional mCRPC patient populations. To this end, we recently re-opened the arm of ARMOR2 evaluating Xtandi-refractory patients in order to enroll up to 21 additional patients and expect to begin enrolling patients in this expansion cohort in the first half of 2016. The expansion of this arm of the study follows a compelling response seen in one Xtandi-refractory patient initially enrolled in ARMOR2. This patient did not show a PSA response until after seven months of galeterone treatment, at which time the patient's PSA level rapidly dropped by over 90 percent and, as of December 31, 2015, has remained at less than 0.1 µg/L for over a year. The PSA response curve of this patient is described in Figure 6 below.

Figure 6: PSA Response of Xtandi-Refractory Patient Enrolled in ARMOR2



None of the Xtandi-refractory or Zytiga-refractory patients enrolled in ARMOR2 remained on study for more than seven months, other than the patient who experienced the PSA response described in Figure 6. We plan to evaluate whether, in patients who have developed acquired resistance to Xtandi following prolonged benefit, longer-term administration of galeterone is required in order to demonstrate clinical benefit with galeterone. We plan to assess reduction in PSA levels and safety in these 21 additional patients.

We also expect to initiate in the first half of 2016 a new Phase 2 clinical trial designed to evaluate galeterone in men whose mCRPC rapidly progressed after initial treatment with either Xtandi or Zytiga. We plan to evaluate all patients enrolled in this open-label trial for the presence of AR-V7 using our clinical trial assay, but AR-V7 positive status is not a criterion for inclusion in the trial.

Galeterone Mechanisms of Action

The androgen receptor signaling pathway is the primary pathway that drives prostate cancer growth and has been implicated in other hormonally driven diseases. The pathway is ordinarily activated by the binding of androgens, such as testosterone and DHT, to the ligand binding domain of androgen receptors in prostate cancer cells. Galeterone disrupts the activation of the pathway through multiple mechanisms of action:

- androgen receptor degradation, which reduces the amount of androgen receptor protein in the tumor cells;
- inhibition of the enzyme CYP17, which blocks the synthesis of testosterone; and
- androgen receptor antagonism, which blocks the binding of testosterone or DHT with the androgen receptor.

To our knowledge, there are no approved drugs or drugs in clinical development, other than galeterone, with multiple mechanisms of action including androgen receptor degradation.

In order to demonstrate galeterone's multiple mechanisms of action, we conducted preclinical studies with respect to each mechanism.

Androgen Receptor Degradation

Galeterone decreases the amount of androgen receptor protein in prostate tumor cells by enhancing degradation of the androgen receptor. This reduces the number of androgen receptors in the tumor cells to which androgen can bind and decreases the sensitivity of androgen responsive cells to androgens. During the ASCO Genitourinary Cancers Symposium held in January 2016, we presented data describing the mechanism by which galeterone induces androgen receptor degradation in forms of the disease that exhibit a full-length androgen receptor, as well as in those with a truncated androgen receptor where the ligand-binding domain is not present, such as in AR-V7 positive and AR^{567es} positive disease. We believe that these and earlier observations suggest that an intact ligand binding domain is not required for galeterone-induced androgen receptor degradation.

To elucidate this galeterone mechanism further, our researchers conducted a series of biochemical and cell-based *in vitro* studies that identified two deubiquitinating enzymes that galeterone selectively inhibits – USP12 and USP46. Neither Zytiga nor Xtandi were shown to inhibit these enzymes. By doing so, galeterone induces androgen receptor degradation through a distinct mechanism that does not exist with other currently available androgen receptor-targeting agents. These new data provide a strong preclinical rationale for galeterone's ability to induce androgen receptor degradation, even in the absence of the ligand binding domain.

The effect of galeterone to reduce androgen receptor levels has also been observed in tumor cell lines and a xenograft model in mice. We have observed this effect of galeterone in varying degrees in prostate cancer cell lines that express non-mutated full-length androgen receptor and multiple forms of androgen receptor alterations, including splice variants such as AR-V7, and point mutations, which are single amino acid mutations in the protein sequence of the androgen receptor.

CYP17 Lyase Inhibition

Like Zytiga, galeterone is an inhibitor of CYP17, a protein with two enzymatic functions: hydroxylase and lyase. Because CYP17 plays a central role in synthesizing the androgens that drive tumor cell growth, CYP17 inhibitors have been developed to treat patients with CRPC. Selectively blocking CYP17 lyase reduces the production of key androgen precursors. However, inhibition of the CYP17 hydroxylase causes an accumulation of certain steroids, such as progesterone, deoxycorticosterone and corticosterone, and a reduction in cortisol, which can result in mineralocorticoid excess. An ideal CYP17 inhibitor will selectively block the lyase function of CYP17 relative to hydroxylase so that these steroids do not accumulate to the extent that they cause mineralocorticoid excess.

We conducted preclinical studies of galeterone and abiraterone to evaluate their relative selectivity with respect to the inhibition of the hydroxylase and lyase functions of CYP17. In these studies, galeterone was shown to selectively block the lyase function of CYP17 relative to the hydroxylase function. In contrast, abiraterone more selectively blocked the hydroxylase function relative to the lyase function, consistent with its published risk for mineralocorticoid excess.

Consistent with these findings, in further preclinical studies in cell cultures, we observed that galeterone inhibited testosterone synthesis comparable to abiraterone, but that abiraterone significantly lowered cortisol levels as compared to galeterone. We believe that this difference is due in part to galeterone's selective inhibition of the lyase function of CYP17.

Androgen Receptor Antagonism

Like Xtandi, galeterone blocks androgens from binding to the androgen receptor. This results in reduced translocation of the androgen receptor into the cell nucleus, which prevents the androgen receptor from acting as a transcription factor and decreases the expression of androgen-responsive genes that drive tumor growth. In *in vitro* studies, galeterone has shown potency of antagonism greater than or comparable to other androgen receptor antagonists, including enzalutamide.

Preclinical Development

We have conducted *in vitro* and *in vivo* preclinical studies to evaluate galeterone's effect on prostate cancer, including the efficacy of galeterone in hormone-sensitive tumor cell lines, in tumors expressing AR-V7 and other splice variants, and in tumors expressing androgen receptor point mutations.

Activity in Hormone Treatment-Resistant Prostate Cancer

We believe that galeterone has the potential to treat tumors that are resistant to hormone treatments because of its differentiated mechanisms of action. In preclinical studies, others have reported key mechanisms of resistance in hormone treatment-resistant prostate cancer, which include:

- increased CYP17 enzyme levels;
- increased production of testosterone and DHT;
- increased wild type or mutant androgen receptor levels;
- alterations in the androgen receptor, such as splice variants and point mutations;
- mutations in the androgen receptor that result in activation by steroids, such as prednisone and progesterone; and
- androgen receptor mutations which convert androgen antagonists into agonists thus leading to activation of the receptor.

Activity in Tumors Expressing Splice Variants, including AR-V7

Androgen receptor splice variants are produced in tumor cells due to an aberrant RNA splicing event. As a result, a truncated androgen receptor protein is synthesized that lacks the C-terminal end of the protein, the region of the protein responsible for androgen binding. Tumor cells that express altered androgen receptors that lack the C-terminal end of the protein are not responsive to agents whose activity requires a functional ligand binding domain. In addition, the lack of the ligand binding domain causes the remaining splice variants to be constitutively active, or continuously signaling, meaning that activation of the androgen receptor pathway and tumor growth occurs even in the absence of androgens and androgen binding. This indicates the importance of androgen receptor degradation to the prevention of tumor growth.

As a follow-up to preclinical studies in which galeterone had caused degradation of full-length androgen receptors, preclinical studies were conducted in independent laboratories to determine whether galeterone also causes androgen receptor degradation in splice variant proteins.

In preclinical studies, we measured androgen receptor degradation using cell lines that expressed full-length and splice variant androgen receptors. These cells model the expression patterns described in human tumor samples where full-length and splice variant androgen receptor proteins are co-expressed. In these studies, levels of both full-length androgen receptor and AR-V7 were reduced in a dose-dependent fashion following galeterone treatment.

To demonstrate that galeterone would degrade the AR-V7 protein alone, in the absence of the full-length androgen receptor, researchers at the University of Maryland, Baltimore, or UMB, studied galeterone in a prostate cancer cell line that only expresses AR-V7, and not the full-length androgen receptor. In these studies, AR-V7 protein levels were reduced in a dose-dependent fashion in cells that only express AR-V7 and not the full-length androgen receptor, confirming that galeterone can act directly on AR-V7.

In addition, together with the Vancouver Prostate Centre, we examined whether degradation of androgen receptors translated into reduced androgen receptor signaling and reduced tumor growth in prostate cancer tumor cells which express AR-V7. The Vancouver Prostate Centre conducted a series of studies evaluating the anti-tumor activity of galeterone and enzalutamide in AR-V7 expressing cells. In these studies, galeterone reduced tumor cell proliferation, reduced androgen receptor levels, and decreased nuclear translocation of the androgen receptor, while enzalutamide was only weakly effective in these measures of anti-tumor activity.

Researchers at the University of Washington also evaluated the *in vivo* activity of galeterone in a LuCaP136 xenograft model of human prostate cancer tumor cells grown in castrated mice. LuCaP136 is a prostate cancer cell line that expresses AR-V7. In these studies, tumors grew in control animals, but castrated animals treated with galeterone showed pronounced tumor growth inhibition.

In addition, researchers at UMB have also evaluated galeterone against a second splice variant, AR^{v567es}. AR^{v567es}, like AR-V7, is a truncated androgen receptor with C-terminal loss. To demonstrate that galeterone would degrade the AR^{v567es} protein alone, in the absence of a full-length androgen receptor, galeterone was studied in a prostate cancer cell line that only expresses AR^{v567es}, and not the full-length androgen receptor. In this study, AR^{v567es} protein levels were reduced in a dose-dependent fashion in cells that only express AR^{v567es} and not the full-length androgen receptor.

Activity in Androgen Receptor Point Mutations

Patients treated with Xtandi and Zytiga eventually develop resistance such that their tumors continue to grow despite continued treatment. In addition, some patients never respond to initial treatment with Zytiga or Xtandi. Preclinical studies have shown that this resistance may be caused by androgen receptor point mutations such as AR-F876L and AR-T878A. In preclinical studies, galeterone was active against prostate cancer cells that expressed these point mutations.

Androgen Receptor Degradation Compounds

Under a license from UMB, we have a drug discovery program, known as ARDA (androgen receptor degradation agents), under which we are identifying and developing novel compounds designed to have potent androgen receptor degradation activity. Our most advanced series of compounds from this program is currently in preclinical development. We plan to target compounds developed under our ARDA program for patients with androgen receptor signaling diseases, including prostate cancer, either alone or in combination with other products.

Manufacturing

Galeterone is a small molecule drug candidate that is manufactured through a reproducible synthetic process from readily available raw materials. Galeterone is manufactured in a proprietary formulation based on spray dried dispersion technology that is designed to produce a product that provides consistent drug exposure.

We have completed the production of formulated drug for use in ARMOR3-SV and our other ongoing and planned clinical trials of galeterone using manufacturers operating under current Good Manufacturing Practices, or cGMP, to manufacture pivotal clinical trial materials.

We do not have our own manufacturing facilities. We currently rely, and expect to continue to rely, on a limited number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates after they are approved. If any of our products are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers and one or more backup manufacturers for the commercial production of those products. We believe that there are a number of qualified manufacturers with which we could enter into commercial supply arrangements. Further, we believe that the process to manufacture galeterone can be scaled up to commercial levels without any unusual equipment.

Commercialization Strategy

We have worldwide development and commercialization rights to galeterone. To maximize the value of these rights, we intend to build a urology- and oncology-focused specialty sales and marketing organization in the United States to support the commercialization of galeterone. We believe that a specialty sales force will be able to target the key prescribing physicians in urology and oncology that treat CRPC. We currently have no sales and limited marketing capabilities and experience. We plan to establish the required capabilities within an appropriate time frame ahead of any product approval and commercialization to support a product launch. To develop the appropriate internal commercial infrastructure in the United States, we will have to invest substantial financial and management resources, some of which will have to be deployed prior to any confirmation that galeterone will be approved. We intend to commercialize galeterone outside the United States through collaborations with third parties.

Under the terms of our agreement with Qiagen, Qiagen is responsible for the commercialization of the AR-V7 companion diagnostic.

Competition

The development and commercialization of new drug products is highly competitive. Research and discoveries by others may result in breakthroughs which may render our products obsolete even before they generate any revenue. We face competition with respect to our lead product candidate, and will face competition with respect to any products that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are

pursuing the development of products for the treatment of the disease indications for which we are developing galeterone. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Many marketed therapies for the indications that we are currently pursuing, or indications that we may in the future seek to address, are widely accepted by physicians, patients and payors, which may make it difficult for us to replace them with any products that we successfully develop and are permitted to market.

We are focusing our late-stage development of galeterone on the treatment of AR-V7 positive mCRPC patients. Based on their mechanisms of action, preclinical data and the data from investigator-initiated clinical trials conducted at several academic medical centers, we believe that Zytiga and Xtandi may be less responsive in patients whose androgen receptor is truncated and do not expect that other drugs in development with similar mechanisms of action will be responsive in this patient population. We expect, however, that other drugs with alternative mechanisms of action may be developed for this patient population.

We believe that galeterone may be well suited to treat other prostate cancer patient populations. If galeterone is approved for additional indications, it may compete with other commonly-used oral hormonal treatments being marketed, such as Zytiga and Xtandi, chemotherapeutic agents, or with drug candidates currently in development. Galeterone could compete in the future with products, either hormonal or non-hormonal, marketed by several of the world's largest and most experienced pharmaceutical companies. These companies have substantially more financial resources than we do and greater flexibility to engage in aggressive price competition to gain revenues and market share. Approved second-generation hormonal treatments in the United States for CRPC include Zytiga, marketed by Janssen Biotech, Inc. and Xtandi, marketed by Astellas Pharma US, Inc. and Medivation, Inc. Approved non-hormonal agents for CRPC include Taxotere® (docetaxel) and Jevtana® (cabazitaxel), marketed by sanofi-aventis U.S. LLC; Provenge® (sipuleucel-T), marketed by Valeant Pharmaceuticals International Inc.; and Xofigo® (radium-223), marketed by Bayer HealthCare Pharmaceuticals, Inc. It is uncertain whether we could compete with such products, and our failure to compete or decision to reduce the price of galeterone or other future products we may develop in order to compete could severely impact our business.

In addition, there are numerous prostate cancer products in clinical development by many public and private biotechnology and pharmaceutical companies targeting numerous different cancer types. These include hormonal treatments such as Johnson & Johnson's ARN-509, Orion Corporation's ODM-201, Innocrin's Pharmaceuticals, Inc.'s VT-464 and Essa Pharma Inc.'s EPI-506. Other compounds that are not hormonal treatments in clinical development include Bavarian Nordic A/S's Prostvac and AstraZeneca plc's olaparib. If a therapy for prostate cancer were developed that targeted the C-terminal loss or AR-V7 patient populations or altered the standard of care for the treatment of mCRPC, such therapy could render galeterone irrelevant.

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render galeterone or any future product candidates obsolete or non-competitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, medical and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We believe the key competitive factors that will affect the development and commercial success of galeterone, if approved, will be efficacy, safety and tolerability profile, probability of drug resistance, convenience of dosage regimen, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Intellectual Property

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, their methods of use, related technology and other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

A third party may hold intellectual property, including patent rights that is important or necessary to commercialize our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms. We may not be able to obtain such licenses on commercially reasonable terms, or at all, in which case our business could be harmed, possibly materially.

We plan to continue to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment and additional compounds and their derivatives. Specifically, we seek patent protection in the United States and internationally for novel compositions of matter covering the compounds, the chemistries and processes for manufacturing these compounds and the use of these compounds in a variety of therapies.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions can be maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention or in post-grant challenge proceedings at the USPTO or at a foreign patent office, such as *inter partes* review and post grant review proceedings at the USPTO and opposition proceedings at the European Patent Office, that challenge priority of invention or other features of patentability. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us.

We generally file a provisional patent application with the USPTO first and then subsequently file a corresponding non-provisional patent application, which enables us to establish an earlier effective filing date in the subsequently filed non-provisional patent application. In order to benefit from the earlier effective filing date, we must file a corresponding non-provisional patent application, such as a utility application in the United States or an international application under the Patent Cooperation Treaty, or PCT, within 12 months of the date of the

provisional patent application filing. Based on the PCT filing, we may file national and regional patent applications in the United States, the European Union, China, Japan, Australia, Canada, Brazil, India, Indonesia, Israel, Mexico, New Zealand, South Korea, Singapore, South Africa or the Eurasian Patent Organization. To date, we have not filed for patent protection in all national and regional jurisdictions where such protection may be available, and we may decide to abandon national and regional patent applications before a patent is granted. In addition, the patent grant proceeding for each national or regional patent application that we file is an independent proceeding. As a result, it is possible for a patent application to be granted in one jurisdiction and denied in another jurisdiction, and depending on the jurisdiction, the scope of patent protection may vary.

Galeterone Patent Portfolio

Our success will depend, in part, on our ability to obtain and maintain patent protection for galeterone and other product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. As of December 31, 2015, we owned three issued U.S. patents, 15 U.S. provisional and non-provisional patent applications, three granted foreign patents and 46 foreign applications in our galeterone patent portfolio. We also had rights under our license agreements with UMB and Johns Hopkins to seven issued U.S. patents and 76 granted foreign patents as well as six U.S. patent applications and 23 foreign applications. Our owned and licensed patent and patent applications, if issued, are expected to expire on various dates from 2017 through 2036, without taking into account any possible patent term extensions. Upon the expiration of these patents, we, UMB and Johns Hopkins, as applicable, will lose the right to exclude others from practicing the inventions claimed by such patents. As a result, the expiration of these patents could have a material adverse effect on our business, results of operations, financial condition and prospects.

We have no patent protection specifically covering the chemical structure of galeterone. As a result, a third party that obtains regulatory approval of a product with the same active ingredient as galeterone may be able to market such product so long as the third party does not infringe any other patents owned or licensed by us with respect to galeterone. For this reason, we have filed for or licensed patents and patent applications relating to galeterone covering methods of use, pharmaceutical compositions, combination treatments, prodrugs, metabolites, and analogs of galeterone and their use.

Method of Use. We have licensed from UMB a U.S. patent covering a method of treating prostate cancer in a human subject by administering galeterone, which is expected to expire in 2027. The license also includes granted patents in the European Patent Convention and Japan covering the use of galeterone to treat prostate disease, including prostate cancer and prostatic hyperplasia. Similar patents have been granted or allowed in Australia, Canada, Hong Kong, South Korea, Mexico, New Zealand, Singapore, South Africa, and the Eurasian Patent Organization. These patents are expected to expire in 2026. In addition, we have pending applications in Brazil, China, India, Israel and Indonesia. We have also licensed from UMB a PCT patent application covering the use of galeterone to inhibit proliferation of a cell having a specific splice variant form of the androgen receptor. The term of a patent derived from this PCT application, if issued, would be expected to expire in 2034.

We have also filed a PCT patent application covering the use of galeterone in treating prostate cancer mediated by androgen receptor variants, including splice variants such as AR-V7, as well as the use of biomarkers in identifying patients who are expected to respond to treatment with galeterone. This application is jointly owned with UMB and the University of Washington, and we have exclusively licensed those institutions' undivided interest in such application and any resulting patents. The term of a patent derived from this PCT application, if issued, would be expected to expire in 2034.

Pharmaceutical Compositions. We have filed U.S. and international patent applications relating to a galeterone formulation and its use where the galeterone is present in a spray dried dispersion. We have pending applications in the United States, the European Union, Australia, Brazil, Canada, China, India and Japan. The term of any patent in this family, if issued, would be expected to expire in 2032. In addition, we have licensed from UMB a U.S. patent application covering a pharmaceutical composition of galeterone. The term of any patent, if issued, claiming priority to this application would be expected to expire in 2026.

Prodrugs, Metabolites and Analogs. We have filed patent applications or licensed from UMB patent applications directed to prodrugs, metabolites or analogs of galeterone. For example, we have licensed a U.S. patent application from UMB directed to certain prodrugs of galeterone. If issued, the term of the resulting patent, if issued, would be expected to expire in 2029. We have also filed patent applications in the United States and certain other countries including Australia, Brazil, Canada, China, the European Union, India and Japan directed to other prodrugs of galeterone. If issued, the term of the resulting patents would be expected to expire in 2030. Further, we have filed patent applications in the United States and certain other countries including Australia, Brazil, Canada, China, the European Union, India and Japan directed to compounds which have been identified as metabolites of galeterone and which may be biologically active. If issued, the term of the resulting patents would be expected to expire in 2030. We have also obtained a license to a UMB PCT patent application directed to analogs of galeterone that disrupt androgen receptor signaling by degrading the androgen receptor. The term of any patent, if issued, claiming priority to this PCT patent application would be expected to extend to 2034.

AR-V7 Specific Assay and Companion Diagnostic Test. We have an exclusive license from Johns Hopkins for patent applications in the United States, Europe, and Canada covering methods of determining whether a subject may respond to androgen therapy, and methods of determining a subject's risk of recurrence of hormone-refractory or hormone-naïve prostate cancer. If issued, the term of the resulting patents would be expected to expire in 2029. These patent applications may provide protection for an AR-V7 specific assay or companion diagnostic test using this assay that we and Qiagen may develop and commercialize. However, these patent applications do not provide any protection for galeterone or for galeterone's pharmaceutical formulations or uses.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property.

License Agreement with University of Maryland, Baltimore

In May 2006, we entered into a master license agreement with UMB. Pursuant to the license agreement, UMB granted us an exclusive worldwide license, with the right to sublicense, under certain patents and patent applications to make, have made, use, sell, offer to sell and import certain anti-androgen steroids including galeterone, which we refer to as licensed products, and to otherwise practice the patent rights in any manner, for the prevention, diagnosis, treatment or control of any human or animal disease. In addition, UMB granted us a first option to receive an exclusive license to UMB's rights in certain improvements to the licensed products, which improvements we refer to as licensed improvements. We have exercised our option and acquired exclusive rights to licensed improvements under three amendments to the license agreement. In March 2009, the license agreement was amended to grant us an exclusive license to oral prodrugs of the licensed products. In April 2012, the license agreement was amended to grant us an exclusive license to compositions and methods of inducing endoplasmic reticulum stress. In October 2013, the license agreement was amended to grant us an exclusive license to a patent application directed to analogs of galeterone that disrupt androgen receptor signaling by degrading the androgen receptor.

Under the terms of the license agreement, as amended, we are obligated to use commercially reasonable efforts to develop and commercialize one or more licensed products. We must also achieve specified milestone events by specified dates. UMB may terminate the agreement if we fail to achieve such milestone events and do not cure such failure within a specified termination notice period. UMB may also terminate the agreement upon our breach of our payment obligations or our other material breaches under the agreement if we do not cure such breach within a specified notice period or upon our bankruptcy or insolvency. We may terminate the agreement at any time, on a country-by-country basis, if we determine that a license under the licensed patent rights in an applicable country is not advantageous to our commercial success, provided that our payment obligations with respect to licensed products in such country would survive termination if we continued to develop and commercialize licensed products in such country following such a termination. Unless our license agreement with UMB is terminated earlier as provided above, our exclusive license from UMB expires on a country-by-country basis as of the later of the expiration date of the last to expire of the claims of the patent rights licensed to us under the agreement in such country or ten years after the first commercial sale of a licensed product in such country.

In consideration for the rights granted to us, we made an upfront payment to UMB of $20,000 following the execution of the license agreement and a payment of $10,000 following the execution of each of the March 2009, April 2012 and October 2013 amendments. We are obligated to pay UMB an annual maintenance fee of $10,000 each year until the first commercial sale. In addition, we paid UMB a $50,000 milestone payment in 2009 upon the submission of our investigational new drug application, or IND, for galeterone and a $40,000 milestone payment in 2013 upon the issuance of the first patent related to UMB's prodrug patent application. We are obligated to make an additional $50,000 milestone payment to UMB for each additional IND we file for a licensed product and a $100,000 milestone payment upon the approval of each NDA for a licensed product by the FDA. We must also pay UMB a low-single digit percentage royalty on aggregate worldwide net sales of licensed products, including sales by our sublicensees, on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last-to-expire applicable licensed patent or ten years after first commercial sale of the applicable licensed product, in each case in the applicable country. Our royalty obligations are subject to specified reductions in the event that we are required to obtain additional licenses from third parties or in the event of specified competition from third-party products licensed by UMB. Our minimum annual royalty payment to UMB is $50,000 beginning in the year following the year in which the first commercial sale occurs. We must also pay UMB 10% of all non-royalty sublicense income received from sublicensees. Finally, as of April 10, 2012, we assumed responsibility for all patent expenses related to the prosecution and maintenance of the licensed patents.

License Agreement with The Johns Hopkins University

In January 2015, we entered into an exclusive license agreement with Johns Hopkins. Pursuant to the license agreement, Johns Hopkins granted us an exclusive worldwide license under certain patent applications and a non-

exclusive license under certain know-how, with the right to sublicense, to make, have made, use, sell, offer to sell and import certain assays to identify androgen receptor variants for use as a companion diagnostic with galeterone. In addition, Johns Hopkins granted us an option to negotiate an exclusive license to Johns Hopkins's rights in certain improvements to the licensed products.

Under the terms of the license agreement, we are obligated to diligently develop, manufacture and sell licensed products. We are also obligated to use commercially reasonable efforts to achieve specified milestone events by specified dates. Unless the license agreement with Johns Hopkins is terminated earlier as provided below, the license from Johns Hopkins expires on a country-by-country basis as of the later of the expiration date of the last to expire of the claims of the patent rights licensed under the agreement in such country or ten years after the first commercial sale of a licensed product in such country. Johns Hopkins may terminate the agreement if we fail to achieve such milestone events and do not cure such failure within a specified termination notice period. Johns Hopkins may also terminate the agreement upon a material breach by us under the agreement if we do not cure such breach within a specified notice period or upon bankruptcy or insolvency. We may terminate the agreement at any time upon 90 days' notice.

In consideration for the rights granted to us under the license agreement, we made an upfront payment to Johns Hopkins of $75,000 following the execution of the license agreement. We are obligated to pay Johns Hopkins an annual minimum royalty of up to $30,000. We are also obligated to make milestone payments to Johns Hopkins upon the achievement of specified technical and commercial milestones. We paid $50,000 during 2015 related to the achievement of two of these milestones. If all such milestones are achieved, the total milestone payments owed to Johns Hopkins would equal in the aggregate $700,000. We must also pay Johns Hopkins single digit percentage royalties on aggregate worldwide net sales of licensed products (and not galeterone), including sales by sublicensees, on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last-to-expire applicable licensed patent or ten years after first commercial sale of the applicable licensed product, in each case in the applicable country. These royalty obligations are subject to specified reductions in the event that additional licenses from third parties are required. We must also pay Johns Hopkins 20% of all non-royalty sublicense income received from sublicensees and reimburse them for patent costs.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, clearance, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products and medical devices. The processes for obtaining regulatory clearances and approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing

review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or IND so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- ***Phase 1:*** The drug is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- ***Phase 2:*** The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- ***Phase 3:*** Phase 3 clinical trials are commonly referred to as "pivotal" trials, which typically denotes a trial which generates the principal data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. In Phase 3 trials, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical trials that must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional studies, trials or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding $2.1 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $104,000 per product and $554,000 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for various reasons, including for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as Active Pharmaceutical Ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may give a product fast track designation if the product is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track designated product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case- by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has

limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug…"

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA applicant or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA

has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Patent Term Restoration and Extension

A patent claiming a new drug product or medical device may be eligible for a limited patent term extension under the FDCA, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a new drug product or medical device is typically one-half the time between the date a clinical investigation on human beings is begun and the submission date of an application for approval of the product, plus the time between the submission date of an application for approval of the product and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product or medical device is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs or medical devices for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Companion Diagnostics in the United States

We expect that we will rely upon an *in vitro* diagnostic test for use in selecting patients with AR-V7. In July 2014, the FDA issued final guidance stating that if an *in vitro* diagnostic is essential to the safe and effective use of a therapeutic product, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product. *In vitro* diagnostics marketed in the United States are regulated as medical devices. As a result, unless an exemption applies, a new medical device may not be marketed in the United States unless and until it has been cleared through filing of a 510(k) premarket notification, or 510(k), or approved by the FDA pursuant to the PMA process. Based on our discussions with the FDA, we believe that the companion diagnostic for galeterone will need to be approved through the PMA process.

510(k) Premarket Notification

To obtain 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is "substantially equivalent" to a predicate device, which is a previously cleared 510(k) device or a pre-amendment device that was in commercial distribution before May 28, 1976, that is a class I or II device, or a class III device for which the FDA has not yet called for the submission of a PMA application. The FDA's 510(k) clearance pathway usually takes from three to 12 months from the date the notification is submitted and filed with the FDA, but it can take significantly longer and clearance is never assured. The FDA has issued guidance documents meant to expedite review of a 510(k) and facilitate interactions between manufacturers and the agency. To demonstrate substantial equivalence, a manufacturer must show that the device has the same intended use as a predicate device and the same technological characteristics, or the same intended use and different technological characteristics and does not raise new questions of safety and effectiveness than the predicate device. Most 510(k)s do not require clinical data for clearance, but the FDA may request such data. If the FDA concludes that the device is not substantially equivalent to a predicate device, the manufacturer will

need to submit a PMA to market the device. Alternatively, a manufacturer may request a *de novo* classification if the device is of low to moderate risk and there is no predicate device upon which to base a substantial equivalence determination.

Premarket Approval

The PMA process for approval to market a medical device is more complex, costly, and time consuming than the 510(k) clearance procedure. A PMA must be supported by extensive data, including technical information regarding device design and development, preclinical studies, clinical studies, manufacturing and controls information and labeling information, which demonstrates the safety and effectiveness of the device for its intended use. The FDA may refer a PMA to an advisory committee for its recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. If the FDA's evaluations of both the PMA and the manufacturing facility for the device are favorable, the FDA will either issue an approval letter authorizing commercial marketing or an approvable letter that usually contains a number of conditions that must be met in order to secure final approval. If the FDA's evaluations are not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years, and the process can be expensive and uncertain. Moreover, even if the FDA approves a PMA, the FDA may approve the device with an indication that is narrower or more limited than originally sought, and the agency may impose post-approval conditions that it believes necessary to ensure the safety and effectiveness of the device.

Investigational Device Exemption

A clinical trial is typically required for a PMA and, in a small percentage of cases, the FDA may require a clinical trial in support of a 510(k) submission. A manufacturer that wishes to conduct a clinical trial involving the device is subject to the FDA's IDE regulation. The IDE regulation distinguishes between significant and nonsignificant risk device trials and the procedures for obtaining approval to begin the trial differ accordingly.

Also, some types of trials are exempt from the IDE regulations. A significant risk device presents a potential for serious risk to the health, safety or welfare of a subject. Significant risk devices are devices that are substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment to human health. Trials of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical trial. Nonsignificant risk devices are devices that do not pose a significant risk to the human subjects. A nonsignificant risk device trial requires only IRB approval prior to initiation of a clinical trial.

An IDE application must be supported by appropriate data, such as animal and laboratory testing results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. An IDE application is considered approved 30 days after it has been received by the FDA, unless the FDA otherwise informs the sponsor, prior to 30 calendar days from the date of receipt, that the IDE is approved, approved with conditions or disapproved. The FDA typically grants IDE approval for a specified number of subjects to be enrolled at specified trial centers. The clinical trial must be conducted in accordance with applicable regulations, including but not limited to the FDA's IDE regulations. The investigators must obtain subject informed consent, rigorously follow the investigational plan and trial protocol, control the disposition of investigational devices, and comply with all reporting and record keeping requirements. A clinical trial may be suspended or terminated by the FDA, the IRB or the sponsor at any time for various reasons, including a belief that the risks to the trial participants outweigh the benefits of participation in the trial. Approval of an IDE does not bind the FDA to accept the results of the trial as sufficient to prove the product's safety and efficacy, even if the trial meets its intended success criteria.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy

and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a drug under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Review and Approval of In Vitro Diagnostics in the European Union

In the European Economic Area, or EEA, *in vitro* diagnostic medical devices are regulated as medical devices and are required to conform with the essential requirements of the E.U. Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). As medical devices, *in vitro* diagnostic medical devices must comply with the Essential Requirements in Annex I to the E.U. Medical Devices Directive (Council Directive 93/42/EEC), or the Essential Requirements. Specifically, a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. Except for low risk medical devices, where the manufacturer can issue a CE Declaration of Conformity based on a self-assessment of the conformity of its products with the Essential Requirements, a conformity assessment procedure requires the intervention of a third-party organization designated by competent authorities of a European Union country to conduct conformity assessments, or a Notified Body. Notified Bodies are independent testing houses, laboratories, or product certifiers typically based within the European Union and authorized by the European member states to perform the required conformity assessment tasks, such as quality system audits and device compliance testing. The Notified Body would typically audit and examine the product's Technical File and the quality system for the manufacture, design and final inspection of the product before issuing a CE Certificate of Conformity demonstrating compliance with the relevant Essential Requirements.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit net revenue and results.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products and devices for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result,

increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country.

Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA, require manufacturers of covered drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Employees

As of December 31, 2015, we had 24 full-time employees and three part-time employees, 14 of whom were primarily engaged in research and development activities.

Corporate Information

We were incorporated under the laws of the State of Delaware on March 26, 2004 under the name Tokai Pharmaceuticals, Inc. Our principal executive office is located at 255 State Street, 6th Floor, Boston, Massachusetts 02109, and our telephone number is (617) 225-4305.

Information Available on the Internet

Our Internet website address is *www.tokaipharmaceuticals.com*. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K. We have included our website address in this in this Annual Report on Form 10-K solely as an inactive textual reference. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through the "SEC Filings" section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at *http://www.sec.gov*.

ITEM 1A. *RISK FACTORS*

Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with the other information included or incorporated by reference in this annual report on Form 10-K. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $45.1 million for the year ended December 31, 2015, $23.3 million for the year ended December 31, 2014 and $15.7 million for the year ended December 31, 2013. As of December 31, 2015, we had an accumulated deficit of $131.4 million. To date, we have financed our operations primarily through our initial public offering of our common stock, and prior to our initial public offering, through private placements of our redeemable convertible preferred stock and convertible promissory notes. We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed development of any product candidate and it may be several years, if ever, before we have a product candidate ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially if and as we:

- conduct ARMOR3-SV, our pivotal Phase 3 clinical trial of galeterone in patients with metastatic castration resistant prostate cancer, or mCRPC, whose prostate tumors express the AR-V7 splice variant, and other clinical trials and non-clinical studies to support the submission of a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for galeterone for this indication;
- develop a companion diagnostic test for use with galeterone in collaboration with Qiagen Manchester Limited, or Qiagen;
- conduct planned additional clinical trials of galeterone in mCRPC patients who have shown resistance following treatment with Xtandi or Zytiga;
- develop galeterone for the treatment of other indications and patient populations in prostate cancer;
- identify and develop compounds that are designed to disrupt androgen receptor signaling through enhanced androgen receptor degradation;
- enter into agreements with third parties to manufacture galeterone;
- establish a sales, marketing and distribution infrastructure to support the commercialization of galeterone in the United States;
- maintain, expand and protect our intellectual property portfolio;
- continue our other research and development efforts;
- acquire or in-license additional compounds or technologies; and
- operate as a public company.

We have never generated any revenue from product sales and may never be profitable. To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential and market acceptance. This development and commercialization will require us to be successful in a

range of challenging activities, including successfully completing ARMOR3-SV and other NDA-enabling studies as well as preclinical testing and clinical trials of any of our future product candidates, obtaining marketing and regulatory approval for these product candidates, successfully developing a companion diagnostic test for use with galeterone, partnering with third parties to manufacture our product candidates in commercial quantities, marketing and selling those products for which we may obtain regulatory approval, and obtaining reimbursement from third-party payors. We may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. The net losses we incur may fluctuate significantly from quarter-to-quarter and year-to-year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our share price to decline. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We will need substantial additional funding to complete our development of, and to commercialize, galeterone for the treatment of AR-V7 positive mCRPC, which funding may not be available on acceptable terms, or at all. If we are unable to raise capital when needed, we may be forced to delay, reduce, terminate or eliminate product development programs, including our commercialization efforts for galeterone for the treatment of these patients and other indications and patient populations and for our future product candidates.

As of December 31, 2015, we had cash and investments of $64.0 million. We expect that our existing cash and investments will only be sufficient to enable us to fund our planned operating expenses and capital expenditure requirements into the first half of 2017. We will need to obtain substantial additional funding in order to complete the development of, and to commercialize galeterone for patients with AR-V7 positive mCRPC and in other indications and patient populations, submit an NDA to the FDA for galeterone, conduct other clinical trials of galeterone, and develop or commercialize any future product candidates. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce, terminate or eliminate our product development programs and our commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the progress and results of ARMOR3-SV and our efforts to complete the clinical development of galeterone and submit an NDA to the FDA and marketing authorization applications to regulatory authorities outside of the United States;
- the progress and results of any additional clinical trials of galeterone that we decide to conduct for the treatment of other indications and patient populations in prostate cancer, including our planned trials in patients whose mCRPC has progressed after treatment with Xtandi of Zytiga;
- the timing and outcome of regulatory review of galeterone for the treatment of AR-V7 positive mCRPC and in any other indication or patient population, and of any other future product candidates;
- the progress and results of the development of a companion diagnostic test for use with galeterone in collaboration with Qiagen;
- the cost of commercialization activities, including product sales, marketing, manufacturing and distribution, for galeterone and our future product candidates for which we receive regulatory approval;
- the development of future product candidates, including our plans to seek to acquire or in-license additional compounds or technologies;
- revenue, if any, received from commercial sales of galeterone and any future product candidates, should any of our product candidates be approved by the FDA or a similar regulatory authority outside the United States;

- our ability to establish collaborations on favorable terms, if at all, particularly arrangements to develop, market and distribute galeterone and any future product candidates outside the United States; and
- the cost of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, galeterone and any future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations, require us to relinquish rights to our technologies or product candidates or divert our management's attention from our operating activities.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, and collaborations, strategic alliances and licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that require liens to be placed on our property and include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or current or future product candidates or to grant licenses on terms that may not be favorable to us. Additional fundraising efforts may also divert our management from their day-to-day activities, which may compromise our ability to develop and commercialize our product candidates.

Risks Related to the Development and Regulatory Approval of Galeterone and Our Future Product Candidates

We depend heavily on the success of our lead product candidate, galeterone, which is in pivotal clinical development for the treatment of AR-V7 positive mCRPC patients. Any failure to successfully develop galeterone for these patients or for other indications or patient populations, or any future product candidates, or significant delays in doing so, would compromise our ability to generate revenue and become profitable.

We currently have no products approved for sale and have only one product candidate, galeterone, in clinical development. We have invested substantially all of our efforts and financial resources in the development of galeterone, for which we are conducting a pivotal Phase 3 clinical trial in treatment-naïve mCRPC patients whose prostate tumors express AR-V7. Our ability to generate product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and commercialization of galeterone for AR-V7 positive mCRPC patients. We also intend to develop galeterone for other indications or patient populations as well as compounds that are designed to disrupt androgen receptor signaling through enhanced androgen receptor degradation. The success of galeterone or other product candidates will depend on several factors, including the following:

- successfully completing clinical trials, including obtaining clinical results that are statistically significant as well as clinically meaningful in the context of the indications for which we are developing galeterone and our future product candidates;

- receiving marketing approvals for our products from the FDA and similar regulatory authorities outside the United States;
- successfully developing a companion diagnostic test for use with galeterone in collaboration with Qiagen;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for galeterone or other product candidates, both in the United States and internationally;
- establishing successful sales and marketing arrangements and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- obtaining commercial acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining adequate reimbursement;
- effectively competing with other therapies;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of our products following regulatory approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize galeterone and our future product candidates, which would materially harm our business.

If clinical trials of galeterone and our future product candidates, including our pivotal Phase 3 clinical trial of galeterone, fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States or are not otherwise successful, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of galeterone and our future product candidates.

Before obtaining regulatory approval for the sale of galeterone and our future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their product candidates.

We are conducting a pivotal Phase 3 clinical trial of galeterone in treatment-naïve mCRPC patients whose prostate tumor cells express AR-V7. We anticipate completing enrollment in this trial by the end of 2016 and having top-line data from the trial by mid-2017. We have entered into a collaboration with Qiagen to develop and commercialize an AR-V7 specific assay as a companion diagnostic for use with galeterone. Our anticipated time to completion of enrollment and to top-line data is subject to our continued ability to initiate clinical trial sites, our ability to recruit eligible patients, the prevalence of patients with the AR-V7 splice variant, the sensitivity of our clinical trial assay in detecting AR-V7 in patients, the satisfaction by AR-V7 positive patients of other eligibility criteria for participation in the trial, and disease progression rates of the patients enrolled in the trial. The rate of patient enrollment in the trial is difficult to predict as we have limited experience recruiting patients with AR-V7 for a clinical trial, and the percentage of mCRPC patients with AR-V7 is subject to widely varying

projections in published literature. Moreover, because we have not previously conducted a clinical trial of galeterone in patients with AR-V7 or conducted a clinical trial using our AR-V7 clinical trial assay, and clinical trials of Xtandi® (enzalutamide) in AR-V7-positive patients have only been conducted in a limited number of patients at single clinical sites, our assumptions concerning patient prevalence and rates of disease progression could be incorrect. In addition, a higher percentage of AR-V7 positive patients than we anticipate may elect not to participate in ARMOR3-SV or fail to meet the other eligibility criteria for participation in the trial. As a result, there can be no assurance that we will fully enroll, have top-line data from or complete the trial when we anticipate.

For drug and biological products, the FDA typically requires the successful completion of two adequate and well-controlled clinical trials to support marketing approval. In the case of galeterone, we intend to seek approval based upon the results of a single pivotal clinical trial. If the results of the trial are not robust, are subject to confounding factors, or are not adequately supported by other study endpoints, the FDA may refuse to approve galeterone based upon a single clinical trial. Thus there can be no guarantee that the FDA will not require additional pivotal clinical trials as a condition for approving galeterone.

Our ARMOR3-SV trial is a randomized, open label clinical trial comparing galeterone to Xtandi in approximately 148 treatment-naïve mCRPC patients whose prostate tumor cells express the AR-V7 splice variant. The primary endpoint of the trial is radiographic progression-free survival, or rPFS, as determined by a blinded, independent central imaging assessment. We have not conducted any clinical trials of galeterone for patients with AR-V7, comparing galeterone to an active comparator drug, or using a primary endpoint of rPFS. As a result, the results of the clinical trials that we have conducted may not be predictive of the outcome of our ARMOR3-SV trial.

Moreover, we are unaware of any completed or currently ongoing pivotal trials of treatments for prostate cancer for which the sole primary endpoint to support initial FDA drug approval was rPFS. In August 2014, we met with the FDA to discuss plans for our ARMOR3-SV trial. At this meeting, the FDA advised us that, in its view, rPFS and the use of rPFS in the mCRPC context is limited by difficulties in bone scan interpretation and the complexity of the criteria used to define progression, each of which creates uncertainty as to the ability of rPFS to predict improvements in morbidity or mortality. The FDA also advised us that if we used rPFS as the sole primary endpoint, this uncertainty would need to be overcome by a statistically persuasive large relative and absolute magnitude of improvement in rPFS as well as internal consistency across secondary endpoints, including a supportive result in overall survival. We cannot be assured as to how the FDA will interpret any rPFS data that we generate in our ARMOR3-SV trial.

If we are required to conduct additional clinical trials or other testing of galeterone or of our future product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for galeterone or our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- be subject to restrictions on how the product is distributed or used; or
- have the product removed from the market after obtaining marketing approval.

If we experience any of a number of possible unforeseen events in connection with our preclinical studies or clinical trials, our ability to conduct further clinical trials of, obtain regulatory approval of or commercialize galeterone or our future product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, preclinical studies or clinical trials that could delay or prevent our ability to conduct further clinical trials, obtain regulatory approval or commercialization of galeterone or our future product candidates. For instance, we experienced delays following our open label, dose escalation Phase 1 clinical trial of galeterone due to the exposure variability associated with the food effect of administering galeterone in capsule formulation and our efforts to reformulate galeterone, which resulted in the development of the spray dried dispersion formulation of galeterone and required us to conduct additional Phase 1 clinical trials. Unforeseen events that could delay or prevent our ability to conduct clinical trials, obtain regulatory approval or commercialize galeterone and our future product candidates include the following:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- preclinical studies and clinical trials of galeterone or our future product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical or clinical trials or abandon product development programs;
- the number of patients required for clinical trials of galeterone or our future product candidates may be larger than we anticipate, patient enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our failure to conduct our clinical trials in accordance with the FDA's good clinical practices or applicable regulatory requirements in other countries;
- Qiagen is unable to develop a companion diagnostic test for use with galeterone and obtain regulatory approval to market the test on a timely basis, or at all;
- we may decide, or regulators or institutional review boards may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements,
- a finding that the participants are being exposed to unacceptable health risks or the occurrence of serious adverse events associated with galeterone or our future product candidates;
- the cost of clinical trials of galeterone and our future product candidates may be greater than we anticipate; and
- the supply or quality of galeterone or our future product candidates or other materials necessary to conduct clinical trials of such product candidates may be insufficient or inadequate.

In addition, the patients recruited for clinical trials of our product candidates may have characteristics that are different than we expect and different than the clinical trials were designed for, which could adversely impact the results of the clinical trials. For example, our patients could develop genetic mutations that are not responsive or are otherwise resistant to galeterone.

Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. In addition to additional costs, significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to commercialize our product candidates.

Galeterone could ultimately prove to be ineffective or unsafe.

As of December 31, 2015, galeterone had been administered to over 250 prostate cancer patients and healthy volunteers in clinical trials. Despite this experience, we have yet to fully explore the safety and efficacy of galeterone. Ultimately, the results of our clinical trials to date, in which galeterone has been well tolerated and showed clinically meaningful reductions in levels of prostate specific antigen, or PSA, a biochemical marker used to evaluate prostate cancer patients for signs of response to therapy, may prove to be incorrect. No assessment of the efficacy, safety or side effects of a product candidate can be considered complete until all clinical trials needed to support a submission for marketing approval are complete, and success in early-stage clinical trials does not mean that subsequent trials will confirm the earlier findings, or that experience with use of a product in large-scale commercial distribution will not identify additional safety or efficacy issues. If we find that galeterone is not safe, or if its efficacy cannot be consistently demonstrated, we may not be able to commercialize, or may be required to cease distribution of, the product. Galeterone may also prove to be substantially identical or inferior to drugs already available, in which case the market for galeterone would be reduced or eliminated.

We are conducting a pivotal Phase 3 clinical trial of galeterone in treatment-naïve mCRPC patients whose tumor cells express AR-V7. We believe that patients' prostate tumor cells may not be responsive to treatment with Zytiga® (abiraterone acetate) and Xtandi, two approved oral therapies for mCRPC, in the presence of C-terminal loss, including AR-V7, but that galeterone, with its mechanism of androgen receptor degradation, may effectively treat these patients. There can be no assurance, however, that our beliefs and assumptions about the effectiveness of galeterone, Zytiga or Xtandi in the treatment of mCRPC patients with C-terminal loss or AR-V7 are accurate. Our belief that patients' prostate tumors may not be responsive to treatment with Zytiga and Xtandi in the presence of C-terminal loss or AR-V7 is based on our understanding of the mechanisms of action of these products, data from clinical trials conducted by researchers at several academic medical centers, and data from preclinical studies conducted by us and independent laboratories. The investigator-initiated clinical studies conducted at these academic medical centers involved a limited number of patients with C-terminal loss or AR-V7 and were conducted in different patient populations, using different protocols and using different and/or unvalidated assays to identify patients with C-terminal loss or AR-V7. The patient populations, protocols and assays used in these investigator-initiated studies may also differ from the patient populations, protocols and assays used in ARMOR3-SV. In addition, it is possible that other factors were present that caused, or contributed to, the poor responsiveness of Zytiga and Xtandi in the presence of C-terminal loss and AR-V7 in the clinical studies. The outcome of preclinical testing and clinical studies may not be predictive of the success of later clinical trials and is often susceptible to varying interpretations and analyses. If Zytiga and Xtandi are found to be more responsive to C-terminal loss or AR-V7 than we anticipate, any clinical trial designed to compare galeterone to Zytiga and Xtandi for this patient population would be less likely to succeed.

Our belief that galeterone may be effective in mCRPC patients with C-terminal loss, including AR-V7, is based on data from preclinical studies and a retrospective subset analysis that identified, in an unvalidated assay, seven treatment-naïve castration resistant prostate cancer, or CRPC, patients in our Phase 2 clinical trial who had truncated androgen receptors with C-terminal loss. We believe that these data support our view that galeterone may be effective in patients without an intact ligand binding domain. There can be no assurance, however, that these data will be predictive of the success of ARMOR3-SV. ARMOR3-SV is the first clinical trial to evaluate galeterone in prospectively identified patients with AR-V7 and has a design that is different than the design of our Phase 2 clinical trial, including primary endpoints that, unlike our earlier trial, are not based on PSA. The failure of ARMOR3-SV to meet its efficacy and safety endpoints would have a material adverse impact on our ability to obtain approval for galeterone and on our business, financial condition and prospects.

If we experience delays or difficulties in the enrollment of patients in our clinical trials, or patients discontinue their participation in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to complete ARMOR3-SV or conduct any other clinical trials if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States.

Our competitors may have ongoing clinical trials for product candidates that could be competitive with galeterone and our future product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- design of the trial protocol;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- trials of other products for similar indications;
- efforts to facilitate timely patient enrollment in clinical trials;
- patient referral practices of physicians;
- alternative products for similar indications;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

In particular, because ARMOR3-SV is focused on AR-V7 positive mCRPC patients and we expect that only a small percentage of mCRPC patients are AR-V7 positive, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. We expect that we may need to screen more than 1,500 patients to identify and enroll the target number of AR-V7 positive patients. Because we have no experience recruiting patients with AR-V7 for a clinical trial and the percentage of mCRPC patients with AR-V7 is subject to widely varying projections in published literature, we cannot be assured our projections for enrollment are accurate. In addition, the clinical trial assay developed for use to identify patients with AR-V7 has not previously been used in a clinical trial setting and its operation may differ from our expectations or be subject to operator variability. Patient enrollment in ARMOR3-SV may also be adversely affected by data that show little or no activity of Xtandi in patients with AR-V7 as patients in the trial will be randomized to the Xtandi arm and the trial will not provide for crossover to galeterone. Moreover, more AR-V7 positive patients than we anticipate may not meet the other eligibility criteria for participation in the trial. Patient enrollment delays in ARMOR3-SV or any of our other future clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients for ARMOR3-SV would result in significant delays. Any significant delays or increases in costs of ARMOR3-SV could result in the need for us to obtain additional funding to complete the trial.

In addition, patients enrolled in our clinical trials may discontinue their participation at any time during the trial as a result of a number of factors, including experiencing adverse clinical events that may or may not be associated with our product candidates under evaluation. We are aware that other late stage trials in CRPC have been adversely affected by discontinuations by patients who prematurely leave the trial in response to an increase in their PSA levels during the trial. It is possible that patients enrolled in ARMOR3-SV may discontinue

participation in the study prior to radiographic progression due to increased PSA levels or other clinical events. The discontinuation of patients in ARMOR3-SV or any one of our other clinical trials may cause us to delay or abandon our trial, require the enrollment of more patients than initially contemplated, or lead to negative or insufficient results to support a filing for marketing and regulatory approval of the applicable product candidate.

If serious adverse or unforeseen side effects are identified during the development of galeterone or our future product candidates, we may need to abandon or limit our development of some or all of our product candidates.

If galeterone or our future product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain indications or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Adverse or unexpected side effects or characteristics of galeterone, whether discovered by us or independently publicized by third parties during clinical trials, could cause an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of galeterone or our future product candidates, require us to conduct additional clinical trials or other tests or studies, and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities.

As of December 31, 2015, nine of the 121 patients enrolled in our Phase 2 clinical trial of galeterone experienced a serious adverse event that was assessed by the investigator as related or possibly related to the administration of galeterone. No single treatment-related serious adverse event occurred in more than one patient. To date, no adverse events have resulted in interruptions or delays of our clinical trials.

In order to develop and commercialize galeterone for the treatment of AR-V7 positive mCRPC patients, we will need to develop and commercialize a companion diagnostic test that can be used to identify these patients. If we or Qiagen are unable to successfully develop, commercialize and obtain approval for a companion diagnostic test, or if there are significant delays in doing so, we may not achieve marketing approval or realize the full commercial potential of galeterone.

We will need to develop and commercialize a companion diagnostic test that sensitively detects AR-V7 in order to seek approval of, and commercialize galeterone for AR-V7 positive mCRPC patients. We have entered into a collaboration with Qiagen to develop an AR-V7 specific clinical trial assay and a companion diagnostic test for use with galeterone to identify mCRPC patients with AR-V7. We have also discussed with the FDA our development strategy and plans for identifying AR-V7 in ARMOR3-SV, including our plans to develop the assay as a companion diagnostic test.

We do not have experience or capabilities in developing, administering, obtaining regulatory approval for, or commercializing companion diagnostic tests and will need to rely in large part on Qiagen to perform these functions. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside of the United States as medical devices and require separate regulatory approval prior to commercialization. We and Qiagen or other third parties may encounter difficulties in developing, administering and obtaining approval for the companion diagnostic test, including issues relating to sample collection, selectivity, specificity, analytical validation, reproducibility or clinical validation, the resolution of which could require us to enroll more patients in ARMOR3-SV than initially contemplated.

If we or Qiagen are unable to successfully develop and obtain approval of a companion diagnostic test, or experience delays in doing so:

- the development of galeterone for AR-V7 positive mCRPC will be adversely affected;
- galeterone may not receive marketing approval on a timely basis or at all; and
- we will not realize the full commercial potential of galeterone if, among other reasons, we are unable to appropriately identify patients with AR-V7.

If any of these events were to occur, our business would be materially harmed.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize galeterone, and our ability to generate revenue will be materially impaired.

Failure to obtain regulatory approval for galeterone for AR-V7 positive mCRPC patients, or for other indications and patient populations, will prevent us from commercializing galeterone for those indications. Although our management team has experience filing and supporting applications necessary to gain regulatory approvals, we have yet to file for or obtain regulatory approval to market galeterone in any jurisdiction. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish galeterone's safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. Galeterone may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

The process of obtaining regulatory approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidate involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of galeterone. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render galeterone commercially unviable.

If we experience delays in obtaining approval or if we fail to obtain approval of galeterone, the commercial prospects for galeterone may be harmed and our ability to generate revenues will be materially impaired.

Even if we complete the necessary clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize galeterone or our future product candidates or the approval may be for a more narrow indication than we expect.

Even if galeterone or any of our future product candidates demonstrate safety and efficacy in clinical trials, regulatory agencies may not complete their review processes in a timely manner or grant regulatory approval at all. Additional delays may result if a regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of galeterone or our future product candidates.

We have obtained fast track designation from the FDA for galeterone for the treatment of mCRPC. However, fast track designation may not actually lead to a faster development, regulatory review or approval process.

If a product is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet needs for this condition, the treatment sponsor may apply for FDA fast track designation. If the fast track designation is obtained, the FDA may initiate review of sections of an NDA, before the application is complete. This "rolling review" is available if the applicant provides, and the

FDA approves, a schedule for submission of the individual sections of the application. In June 2012, the FDA notified us that we had obtained fast track designation for galeterone for the treatment of mCRPC. Fast track designation does not ensure that we will experience a faster development, regulatory review or approval process compared to conventional FDA procedures or that we will ultimately obtain regulatory approval of galeterone. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

In the event we receive FDA approval for galeterone for AR-V7 positive mCRPC patients, we will not be able to expand the indications for which galeterone is approved unless we receive FDA approval for each additional indication. Failure to expand these indications will limit the size of the commercial market for galeterone.

We are focusing our initial development of galeterone on the treatment of AR-V7 positive mCRPC patients and plan to seek marketing and regulatory approvals for galeterone for this patient population. We also plan to develop galeterone for the treatment of other indications and patient populations in prostate cancer. In order to market and sell galeterone in the United States for these additional indications, we will need to conduct additional clinical trials and obtain FDA approval for each proposed indication. There can be no assurance that we will be successful in obtaining FDA approval for additional indications for the use of galeterone. If we are unsuccessful in expanding the approved indications for the use of galeterone, the size of the commercial market for galeterone will be limited.

Failure to obtain regulatory approval in international jurisdictions would prevent galeterone or our future product candidates from being marketed abroad.

In order to market and sell our products in jurisdictions outside the United States, we or third parties must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval process varies among countries and can involve additional testing. The time required to obtain foreign approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be separately approved for reimbursement before the product can be approved for sale in that country. We intend to enter into arrangements with third parties under which they would market our products outside the United States. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Risks Related to the Commercialization of Our Product Candidates

We have no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We have never commercialized a product candidate. Our operations to date have been limited to financing and staffing our company, developing our product candidates and conducting our preclinical studies and clinical trials. We have not completed a pivotal clinical trial, obtained marketing approvals or conducted sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We may also encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. In the future, we will need to transition from a company with a preclinical and clinical development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Even if galeterone receives regulatory approval, it may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if galeterone receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. If galeterone does not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of galeterone or any of our future product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer galeterone and our future product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- our understanding of the market and development of an effective commercial strategy;
- the strength of sales, marketing, medical affairs and distribution support;
- the approval of other products for the same indications;
- combinations of existing or newly approved products that alter the standard of care;
- availability and amount of reimbursement from government payors, managed care plans and other third-party payors;
- adverse publicity about the product or favorable publicity about competitive products;
- clinical indications for which the product is approved; and
- the prevalence and severity of any side effects.

Even if a potential product candidate displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community, patients and third-party payors on the benefits of galeterone or our other future product candidates may require significant resources and may never be successful.

If galeterone or any of our future product candidates receives marketing approval and we, or others, later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the product could be compromised.

Clinical trials are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect in a broader patient population or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product or change the way the product is administered;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;

- we may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- additional restrictions may be imposed on the distribution or use of the product via a Risk Evaluation and Mitigation Strategy;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing galeterone or any of our future product candidates if they are approved.

We do not have a sales or marketing infrastructure and have limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either outsource these functions to third parties or develop an internal sales and marketing organization. If galeterone is approved in the United States, we intend to build a urology and oncology focused, specialty sales organization in the United States to support the commercialization of galeterone. We intend to commercialize galeterone outside the United States through collaborations with third parties. Such reliance on third parties to market our products, if approved, is risky as these parties may not perform satisfactorily or at all.

There are risks involved with both entering into arrangements with third parties to perform these services and establishing our own sales and marketing capabilities, neither of which we have pursued previously. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retrain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain an adequate number of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these products are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market galeterone or our future product candidates or doing so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing galeterone or our future product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. Research and discoveries by others may result in breakthroughs which may render our products obsolete even before they generate any revenue. We face competition with respect to our lead product candidate, and will face competition with respect to any products that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing galeterone. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Many marketed therapies for the indications that we are currently pursuing, or indications that we may in the future seek to address, are widely accepted by physicians, patients and payors, which may make it difficult for us to replace them with any products that we successfully develop and are permitted to market.

We are focusing our late-stage development of galeterone on the treatment of AR-V7 positive mCRPC patients. Based on their mechanisms of action, preclinical data and the data from investigator-initiated clinical trials conducted at several academic medical centers, we believe that Zytiga and Xtandi may be less responsive in patients whose androgen receptor is truncated and do not expect that other drugs in development with similar mechanisms of action will be responsive in this patient population. We expect, however, that other drugs with alternative mechanisms of action may be developed for this patient population.

We believe that galeterone may be well suited to treat other prostate cancer patient populations. If galeterone is approved for additional indications, it may compete with other commonly-used oral hormonal treatments being marketed, such as Zytiga and Xtandi, chemotherapeutic agents, or with drug candidates currently in development. Galeterone could compete in the future with products, marketed by several of the world's largest and most experienced pharmaceutical companies. These companies have substantially more financial resources than we do and greater flexibility to engage in aggressive price competition to gain revenues and market share. Approved second-generation hormonal treatments in the United States for CRPC include Zytiga, marketed by Janssen Biotech, Inc. and Xtandi, marketed by Astellas Pharma US, Inc. and Medivation, Inc. Approved non-hormonal agents for CRPC include Taxotere® (docetaxel) and Jevtana® (cabazitaxel), marketed by sanofi-aventis U.S. LLC; Provenge® (sipuleucel-T), marketed by Valeant Pharmaceuticals International Inc.; and Xofigo® (radium-223), marketed by Bayer HealthCare Pharmaceuticals, Inc. It is uncertain whether we could compete with such products, and our failure to compete or decision to reduce the price of galeterone or other future products we may develop in order to compete could severely impact our business.

In addition, there are numerous prostate cancer products in clinical development by many public and private biotechnology and pharmaceutical companies targeting numerous different cancer types. These include hormonal treatments such as Johnson & Johnson's ARN-509, Orion Corporation's ODM-201, Innocrin Pharmaceuticals Inc.'s VT-464 and Essa Pharma's Inc.'s EPI-506. Other compounds that are not hormonal treatments in clinical development include Bavarian Nordic A/S's Prostvac and AstraZeneca plc's olaparib. If a therapy for prostate cancer were developed that targeted the C-terminal loss or AR-V7 patient populations or altered the standard of care for the treatment of mCRPC, such therapy could render galeterone irrelevant.

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render galeterone or any future product candidates obsolete or non-competitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, medical and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize galeterone or any other future product candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. In the United States, recently passed legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in galeterone or our future product candidates, even if our product candidates obtain regulatory approval.

Our ability to commercialize any products successfully will also depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we receive marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we receive marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of galeterone and our future product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Galeterone has not been widely used over an extended period of time, and therefore our safety data are limited.

If we cannot successfully defend ourselves against claims that galeterone or future product candidates or products we may develop caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We currently hold $5 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when we begin commercializing galeterone and our future product candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. We remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for galeterone or other product candidates we may develop in the future and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We may enter into collaborations with third parties for the development and commercialization of galeterone and future product candidates we may develop. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may enter into collaborations with third parties for the development and commercialization of galeterone and future product candidates we may develop. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. We will likely have limited control under any additional arrangements we may enter into with third parties over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products;
- are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may have the right to conduct clinical trials of our product candidates without our consent and could conduct trials with flawed designs that result in data that adversely affect our clinical trials, our ability to obtain marketing approval for our product candidates or market acceptance of our product candidates;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish collaborations, we may have to alter our development and commercialization plans.

We will face significant competition in seeking appropriate collaborators if we determine to do so. Whether we reach a definitive agreement for a collaboration will depend upon, among other things, our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Such factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for galeterone. We may also be restricted under existing license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all.

If we are not able to enter into collaborations for galeterone, we may have to curtail the development of galeterone, reduce or delay our development program or one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop galeterone or other future candidates or bring these product candidates to market and generate product revenue.

Failure of Qiagen to successfully develop or commercialize a companion diagnostic test for use with galeterone to identify AR-V7 positive mCRPC patients could harm our ability to commercialize galeterone.

We do not plan to internally develop a companion diagnostic test to identify AR-V7 positive mCRPC patients and, as a result, we will be dependent on the efforts of Qiagen to successfully develop and commercialize this test. Qiagen:

- may not perform its obligations as expected or as required under our agreement with Qiagen;
- may encounter production difficulties that could constrain the supply of the companion diagnostic test;
- may have difficulties gaining acceptance of the use of the companion diagnostic test in the clinical community;
- may not pursue commercialization of the companion diagnostic test even if they receive any required regulatory approvals;
- may elect not to continue the development of the companion diagnostic test based on changes in the third parties' strategic focus or available funding, or external factors such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of the companion diagnostic test; and
- may terminate their relationship with us.

If the companion diagnostic test that is developed for use with galeterone fails to gain market acceptance, our ability to derive revenues from sales from galeterone would be harmed. If Qiagen or any other third parties

we engage fail to commercialize the companion diagnostic test, we may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative test for use with galeterone or do so on commercially reasonable terms, which could adversely affect and delay the development or commercialization of galeterone.

If galeterone is approved, we intend to rely on third parties to perform many necessary services related to the sale and distribution of galeterone, and expect to do so for any future product candidates.

If galeterone is approved, we intend to retain third-party service providers to perform a variety of functions related to the sale and distribution of galeterone, key aspects of which are out of our direct control. For example, we intend to rely on third parties to provide key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management, and storage, including entrusting our inventories of galeterone to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical damage or natural disaster at their facilities, our ability to deliver galeterone to meet commercial demand would be significantly impaired. In addition, we intend to utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to market galeterone could be jeopardized or we could be subject to regulatory sanctions. We do not currently have the internal capacity to perform these important commercial functions, and we may not be able to maintain commercial arrangements for these services on reasonable terms.

Risks Related to the Manufacturing of Galeterone and Our Future Product Candidates

We contract with third parties for the manufacture of galeterone for clinical trials and expect to continue to do so in connection with the commercialization of galeterone and for clinical trials and commercialization of any other product candidates that we develop. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have nor do we plan to build the internal infrastructure or capability to manufacture galeterone. We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture clinical supplies of galeterone and any other product candidates we may develop. We expect to continue to rely upon third-party contract manufacturers to manufacture commercial quantities of galeterone and any other product candidates that we commercialize following approval for marketing by applicable regulatory authorities. Reliance on third-party manufacturers entails risks, including:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely on a small number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our clinical trials. We do not have long-term agreements with any of these third parties. If any of our existing manufacturers should become unavailable to us for any reason, we may incur some delay in our clinical trials as we identify or qualify replacements.

We currently rely on a single third-party contract manufacturer, with which we do not have a long-term agreement, to supply us with the spray dried dispersion formulation of galeterone. If this third-party manufacturer fails to fulfill orders or should become unavailable to us for any reason, we likely would incur some delay in our clinical trials for galeterone and added costs and delays in identifying or qualifying such replacements. In addition, we may be unable to establish any agreements with such replacement manufacturers or to do so on acceptable terms or at all. Even if we could transfer manufacturing to a different third party, the shift would likely be expensive and time-consuming.

If galeterone or any other product candidate that we may develop in the future is approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time-consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under current good manufacturing processes, or cGMPs, that are capable of manufacturing our product candidates. As a result, we may be unable to reach agreement with third-party manufacturers on satisfactory terms or at all, which could delay our commercialization.

Our current and anticipated future dependence upon others for the manufacture of galeterone and any other product candidate that we develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

If our third-party manufacturers' facilities are damaged or destroyed, or production at one of these facilities is otherwise interrupted, our business and prospects would be negatively affected.

If any manufacturing facilities owned by third parties who manufacture galeterone or any of our future product candidates are damaged or destroyed, we likely would not be able to quickly or inexpensively replace our manufacturing capacity and possibly would not be able to replace it at all. Any new facility needed to replace these facilities would need to comply with the necessary regulatory requirements and need to be tailored to our specialized manufacturing requirements. We would need FDA approval before selling any products manufactured at a new facility. Such an event could delay our clinical trials or, if any of our product candidates are approved by the FDA, reduce or eliminate our product sales.

While we maintain insurance coverage to cover damage to our property and equipment and to cover business interruption and research and development restoration expenses, if we have underestimated our insurance needs with respect to an interruption in our clinical manufacturing of our product candidates, we may not be able to adequately cover our losses.

We rely on our third-party manufacturers for compliance with applicable regulatory requirements. This may increase the risk of sanctions being imposed on us or on a manufacturer of our products or product candidates, which could result in our inability to obtain sufficient quantities of these products or product candidates.

Our manufacturers may not be able to comply with cGMPs, regulations or other regulatory requirements or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including:

- fines;
- injunctions;
- civil penalties;
- failure of regulatory authorities to grant marketing approval of our product candidates;
- delays, suspension or withdrawal of approvals;

- suspension of manufacturing operations;
- license revocation;
- seizures or recalls of products or product candidates;
- operating restrictions; and
- criminal prosecutions.

Any of these sanctions could significantly and adversely affect supplies of our products and product candidates.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a master license agreement with the University of Maryland, Baltimore, or UMB, under which we license certain patents and patent applications to make, have made, use, sell, offer to sell and import certain anti-androgen compounds, including galeterone, and an exclusive, worldwide license with Johns Hopkins under which we license patents, patent applications and know-how covering certain assays to identify androgen receptor variants for use as a companion diagnostic with galeterone. We may enter into additional license agreements in the future. Our license agreements with UMB and Johns Hopkins impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could materially adversely affect the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms.

Restrictions on our patent rights relating to our drug candidates may limit our ability to prevent third parties from competing against us.

Our success will depend, in part, on our ability to obtain and maintain patent protection for galeterone and other product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. As of December 31, 2015, we owned three issued U.S. patents, 15 U.S. provisional and non-provisional patent applications, three granted foreign patent and 46 foreign applications in our galeterone patent portfolio. We also had rights under our license agreements with UMB and Johns Hopkins to seven issued U.S. patents and 76 granted foreign patents as well as six U.S. patent applications and 23 foreign applications. Our owned and licensed patent and patent applications, if issued, are expected to expire on various dates from 2017 through 2036, without taking into account any possible patent term extensions. Upon the expiration of these patents, we, UMB and Johns Hopkins, as applicable, will lose the right to exclude others from practicing the inventions claimed by such patents. As a result, the expiration of these patents could have a material adverse effect on our business, results of operations, financial condition and prospects.

Patent applications in the United States and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we and the inventors of the intellectual property for which we have submitted patent applications or in-license issued patents and applications, were the first to conceive of the inventions covered by such patents and pending patent applications or that we and those inventors were the first to file patent applications covering such inventions. Also, the patent protection of our

numerous issued and pending patent applications may lapse before we manage to obtain commercial value from them, which might result in increased competition and materially affect our position in the market.

We have no patent protection specifically covering the chemical structure of galeterone. As a result, a third party that obtains regulatory approval of a product with the same active ingredient as galeterone may be able to market such product so long as the third party does not infringe any other patents owned or licensed by us with respect to galeterone. A U.S. patent we have exclusively licensed from UMB covering galeterone-related compounds and their use expires in 2017. For this reason, we have filed for or licensed additional patents and patent applications relating to galeterone covering methods of use, pharmaceutical compositions, combination treatments, prodrugs, metabolites and analogs of galeterone and their use.

We also have an exclusive license from Johns Hopkins for patents and patent applications in the United States, Europe, and Canada covering methods of determining whether a subject may respond to androgen therapy, and methods of determining a subject's risk of recurrence of hormone-refractory or hormone-naïve prostate cancer that are expected to expire in 2029. These patents applications may provide protection for an AR-V7 specific assay or a companion diagnostic test using this assay that we and Qiagen may develop and commercialize. However, these patent applications do not provide any protection for galeterone or for galeterone's pharmaceutical formulations or uses.

If we are unable to obtain and maintain patent protection for our technology and products, or if our licensors are unable to obtain and maintain patent protection for the technology or products that we license from them, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We and our licensors have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development efforts before it is too late to obtain patent protection. Moreover, prior to April 10, 2012, we did not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or products that we license from UMB, and we were and still are reliant on UMB. Therefore, we cannot be certain that these patents and applications were prosecuted in a manner consistent with the best interests of our business. If we or our licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued that protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Third parties could practice our inventions in territories where we do not have patent protection. Furthermore, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. A U.S. patent may be infringed by anyone who, without authorization, practices a patented process in the United States or imports a product made by a process covered by the U.S. patent. In foreign countries, however, importation of a product made by a process patented in that country may not constitute an infringing activity, which would limit our ability to enforce process patents against importers in that country. Furthermore, the legal

systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection. This could make it difficult for us to stop the infringement or misappropriation of our intellectual property rights. If competitors are able to use our technologies, our ability to compete effectively could be harmed.

Assuming the other requirements for patentability are met, in the United States, the first to invent the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is generally entitled to the patent. Under the America Invents Act, or AIA, enacted in September 2011, the United States moved to a first inventor to file system in March 2013. The U.S. Patent and Trademark Office recently finalized the rules relating to these changes and courts have yet to address the new provisions. These changes could increase the costs and uncertainties surrounding the prosecution of patent applications and the enforcement or defense of patent rights. Furthermore, we may become involved in interference proceedings, opposition proceedings, or other post-grant proceedings, such as reexamination or *inter partes* review proceedings, challenging our patent rights or the patent rights of others. An adverse determination in any such proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges, including through opposition or other post-grant proceedings, may result in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to or stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to galeterone but that are not covered by the claims of our patents;
- the galeterone compound may become generic, and no patent protection will be available without regard to formulation or method of use;
- we or our licensors, as the case may be, may not be able to detect infringement against our owned or in-licensed patents, which may be especially difficult for manufacturing processes or formulations;
- we or our licensors, as the case may be, might not have been the first to make the inventions covered by our owned or in-licensed issued patents or pending patent applications;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions or the first to conceive or reduce to practice these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- this may be especially likely for manufacturing processes or formulations;

- it is possible that our pending patent applications will not result in issued patents;
- it is possible that our owned or in-licensed issued patents or pending patent applications are not Orange Book eligible;
- it is possible that there are dominating patents to galeterone of which we are not aware;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' inventions, as the case may be, or parts of our or their inventions of which we or they are not aware;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- it is possible that the U.S. government may exercise any of its statutory rights to our owned or in-licensed patents or patent applications that was developed with government funding;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, or may be narrowed in scope, be held invalid or unenforceable as a result of legal challenges by third parties; or
- we may not develop additional proprietary technologies for which we can obtain patent protection.

We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents. To counter such infringement or unauthorized use, we may be required to file infringement claims against third parties, which can be expensive and time-consuming. In addition, during an infringement proceeding, a court may decide that the patent rights we are asserting are invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, our licensors may have rights to file and prosecute such claims, and we are reliant on them.

Claims that galeterone or the manufacture, use or sale of galeterone infringe the patent rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.

We cannot guarantee that galeterone, its manufacture, use or sale, does not and will not infringe third-party patents. Third parties might allege that we are infringing their patent rights or that we have misappropriated their trade secrets. Such third parties might resort to litigation against us. The basis of such litigation could be existing patents or patents that issue in the future.

It is also possible that we failed to identify relevant third-party patents or applications. For example, certain U.S. patent applications that will not be filed outside the United States may remain confidential until patents issue. Furthermore, patent applications in the United States and elsewhere are published approximately

18 months after the earliest filing, which is referred to as the priority date. Therefore, patent applications covering galeterone, its manufacture, use or sale, could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover galeterone or its use.

We are aware of two issued U.S. patents having broad claims relating to a composition of matter or its use in regulating cellular differentiation or proliferation. We are also aware of certain third-party pending U.S. patent applications that have broad generic disclosures and disclosure of certain compounds possessing structural similarities to galeterone. Although we believe that it is unlikely that such applications will lead to issued claims that would cover galeterone and its use and still be valid, patent prosecution is inherently unpredictable and an application could be allowed. Based on our analyses, we do not believe our proposed products or activities would be found to infringe any valid claims of these patents if any of the above third-party patents or patent applications, if issued, were asserted against us. If we were to challenge the validity of an issued U.S. patent in court, however, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that, in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

In order to avoid or settle potential claims with respect to any patent rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be non-exclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing galeterone, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time-consuming, regardless of the outcome. Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent or trade secret litigation longer than we could. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology, or enter into strategic partnerships that would help us bring our product candidates to market.

We may be subject to claims that our employees or directors have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees and certain of our directors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and directors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or directors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or director's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties in the discovery, development and manufacture of our product candidates, and because we collaborate with various organizations and academic institutions on the advancement of our technology, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite these contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by potential competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, discovery by a third party of our trade secrets or other unauthorized use or disclosure would impair our intellectual property rights and protections in our product candidates.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

In addition, our third party agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication.

Risks Related to Compliance Matters

Any product candidate for which we receive marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, if any of them are approved.

Any product candidate for which we receive marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. Even if regulatory approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved label. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing.

In addition, later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have adverse consequences, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, program exclusion, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we receive marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we receive marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, require manufacturers of covered drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that

our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize galeterone or other future products candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of galeterone or other future products candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we receive marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class in certain cases. Cost reduction initiatives and other provisions of this and other more recent legislation could decrease the coverage and reimbursement that is provided for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act or other more recent legislation may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of galeterone or our other future products candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Jodie Morrison, our President and Chief Executive Officer, as well as the other members of our executive and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our research and development, manufacturing and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research and development, manufacturing and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train

additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock

Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, in the aggregate, beneficially own shares representing approximately 66% of our common stock, based on the number of shares of our common stock outstanding as of December 31, 2015. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

We believe our two largest stockholders, Apple Tree Partners and Novartis BioVentures, Ltd., in the aggregate, beneficially own shares representing approximately 55% of our common stock in the aggregate, based on the number of shares of our common stock outstanding as of December 31, 2015. As a result, each of these stockholders acting individually, as well as together, may exercise significant control over our management and affairs.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

An active trading market for our common stock may not be sustained, and investors may not be able to resell their shares at or above the price they paid.

Although we have listed our common stock on The NASDAQ Global Market, an active trading market for our shares may not be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the prices at which they acquired their shares or at the time that they would like to sell. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Our stock price has been and may in the future be volatile, which could cause purchasers of our common stock to incur substantial losses.

Our stock price has been and in the future may be subject to substantial volatility. The stock market in general and the market for biotechnology companies in particular has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. For example, our stock traded within a range of a high price of $30.00 per share and a low price of $4.93 per share for the period beginning September 17, 2014, our first day of trading on The NASDAQ Global Market, through February 29, 2016. As a result of this volatility, our stockholders could incur substantial losses. The market price for our common stock may be influenced by many factors, including:

- results of clinical trials of galeterone and our future product candidates or those of our competitors;
- the success of competitive products or technologies;
- potential approvals of galeterone or other future product candidates for marketing by the FDA or equivalent foreign regulatory authorities or our failure to obtain such approvals;
- regulatory or legal developments in the United States and other countries;
- the results of our efforts to commercialize galeterone or other future products candidates;
- developments or disputes concerning patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to galeterone or any of our future product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts' reports or recommendations;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In addition, pharmaceutical companies have experienced significant share price volatility in recent years, and securities class action litigation often follows a decline in the market price of a company's securities. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources.

We must maintain effective internal control over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could have a material adverse effect on our business and stock price.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a public company, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requires, among other things, that we assess the effectiveness of our disclosure controls and procedures quarterly and the effectiveness of our internal control over financial reporting at the end of each fiscal year.

The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These standards require that our audit committee be advised and regularly updated on management's review of internal control over financial reporting. Our management may not be able to effectively and timely implement controls and procedures that adequately respond to the increased regulatory compliance and reporting requirements that are applicable to us as a public company. If we fail to staff our accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the demands that are placed upon us as a public company, including the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed and our stock price may decline. Furthermore, investor perceptions of us may be adversely affected, which could cause a decline in the market price of our common stock.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years from the date of our initial public offering, although circumstances could cause us to lose that status earlier. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

If equity research analysts do not publish research reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock will rely in part on the research and reports that equity research analysts publish about us and our business. We do not have any control over these analysts. The price of our common stock could decline if we do not obtain research analyst coverage, or one or more securities analysts downgrade our common stock or if those analysts issue other unfavorable commentary or cease publishing reports about us or our business.

ITEM 1B. *UNRESOLVED STAFF COMMENTS*

None.

ITEM 2. *PROPERTIES*

We conduct our operations in leased facilities. We currently lease 15,981 square feet of office space in Boston, Massachusetts under a sublease agreement with Boston Private Wealth LLC. The sublease is subject and subordinate to a prime lease, dated October 5, 2010, with the prime landlord, 255 State Street, LLC. The sublease expires on December 31, 2016. However, if the term of the prime lease is terminated for any reason prior to the expiration or earlier termination of the sublease, the sublease will immediately terminate and we will have no recourse against the sublandlord for such termination. Under the sublease, we are obligated to pay approximately $45,300 per month in lease payments through March 30, 2016 and, beginning on April 1, 2016, we are obligated to pay approximately $46,600 per month in lease payments through December 31, 2016.

In June 2015, we entered into a lease for our existing office space that effectively extends our current lease term from December 2016 until July 2018. Under this lease, we are obligated to pay approximately $69,900 per month in lease payments from January 2017 through July 2018.

ITEM 3. *LEGAL PROCEEDINGS*

We are not currently a party to any material legal proceedings.

ITEM 4. *MINE SAFETY DISCLOSURES*

Not applicable.

PART II

ITEM 5. ***MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES***

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "TKAI" on the NASDAQ Global Market and has been publicly traded since September 17, 2014. Prior to this time, there was no public market for our common stock The following table sets forth the high and low sales price of our common stock as reported on the NASDAQ Global Market for the periods indicated:

	High	Low
Year ended December 31, 2014:		
Third Quarter (beginning September 17, 2014)	$30.00	$15.10
Fourth Quarter	$17.87	$ 9.67
Year ended December 31, 2015:		
First Quarter	$16.10	$11.10
Second Quarter	$14.45	$ 9.77
Third Quarter	$14.71	$ 9.95
Fourth Quarter	$12.93	$ 8.50

Holders of Our Common Stock

As of February 29, 2016, there were approximately 16 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

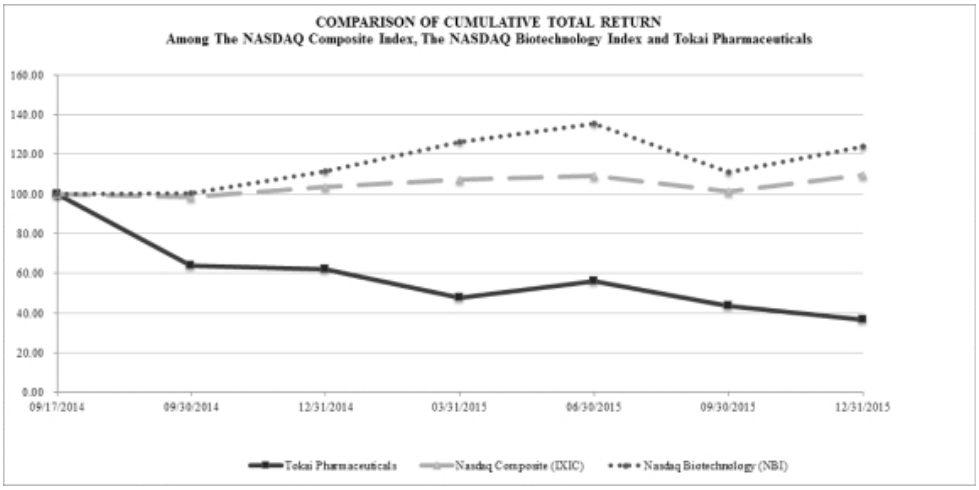
Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay any cash dividends to the holders of our common stock in the foreseeable future.

Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission, or SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Exchange Act or Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to the NASDAQ Composite Index and to the NASDAQ Biotechnology Index from September 17, 2014 (the first date that shares of our common stock were publicly traded) through December 31, 2015. The comparison assumes $100 was invested in our common stock and in each of the foregoing indices after the market closed on September 17, 2014, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



Use of Proceeds from Registered Securities

On September 22, 2014, we completed the initial public offering of our common stock through the issuance and sale of 6,480,000 shares of our common stock at a price to the public of $15.00 per share. In addition, on October 9, 2014, we issued and sold an additional 540,000 shares of common stock at the initial public offering price of $15.00 per share as a result of the partial exercise by the underwriters of their option to purchase additional shares of common stock.

The offer and sale of all of the shares in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-198052), which was declared effective by the SEC on September 16, 2014, and a registration statement on Form S-1MEF (File No. 333-198792), which was automatically effective upon filing with the SEC on September 16, 2014. Following the sale of the shares in connection with the closing of our initial public offering, the offering terminated. The offering commenced on September 16, 2014 and did not terminate until the sale of all of the shares offered.

We received aggregate gross proceeds from the offering of $105.3 million, or aggregate net proceeds of $94.6 million after deducting underwriting discounts and commissions and offering expenses. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any of our affiliates.

As of December 31, 2015, we estimate that we have used approximately $50.7 million of the net proceeds from our initial public offering to fund the clinical development of galeterone and for working capital and other general corporate purposes. We have invested the unused proceeds from the offering in marketable securities and money market accounts. There has been no material change in our planned use of the net proceeds from our initial public offering as described in our final prospectus filed with the SEC on September 17, 2014 pursuant to Rule 424(b)(4) under the Securities Act.

ITEM 6. *SELECTED FINANCIAL DATA*

The selected statements of operations data for the years ended December 31, 2015, 2014 and 2013 and the balance sheet data as of December 31, 2015 and 2014 have been derived from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The selected statements of operations data for the year ended December 31, 2012 and the balance sheet data as of December 31, 2013 and 2012 are derived from our audited consolidated financial statements not included in this Annual Report on Form 10-K. The selected financial data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes, included elsewhere in this Annual Report on Form 10-K. The historical results are not necessarily indicative of the results to be expected in any future period.

	Year Ended December 31,			
	2015	2014	2013	2012
	(in thousands, except share and per share data)			
Consolidated Statement of Operations Data:				
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development (1)	32,638	14,577	12,201	7,370
General and administrative (1)	12,623	8,885	3,548	2,279
Total operating expenses	45,261	23,462	15,749	9,649
Loss from operations	(45,261)	(23,462)	(15,749)	(9,649)
Interest and other income (expense), net	174	166	24	—
Net loss	(45,087)	(23,296)	(15,725)	(9,649)
Accretion of redeemable convertible preferred stock to redemption value	—	—	(94)	(34)
Net loss attributable to common stockholders	$ (45,087)	$ (23,296)	$ (15,819)	$ (9,683)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.01)	$ (3.60)	$ (38.02)	$ (31.09)
Weighted average common shares outstanding, basic and diluted	22,484,343	6,469,289	416,037	311,474

(1) Amounts include stock-based compensation expense, as follows:

	Year Ended December 31,			
	2015	2014	2013	2012
	(in thousands)			
Research and development	$ 634	$ 552	$ 91	$ 87
General and administrative	2,267	1,556	147	123
	$ 2,901	$ 2,108	$ 238	$ 210

	As of December 31,			
	2015	2014	2013	2012
	(in thousands)			
Consolidated Balance Sheet Data:				
Cash and investments	$63,957	$105,256	$ 31,753	$ 11,691
Working capital	61,008	103,268	29,969	9,908
Total assets	67,974	107,744	32,287	11,962
Redeemable convertible preferred stock	—	—	85,345	49,845
Total stockholders' equity (deficit)	61,724	103,501	(55,267)	(39,901)

ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the ''Risk Factors'' section of this Annual Report on Form 10-K, our actual results could differ materially from the results described, in or implied, by these forward-looking statements.

Overview

We are a biopharmaceutical company focused on developing and commercializing innovative therapies for prostate cancer and other hormonally driven diseases. Our lead drug candidate, galeterone, is an oral small molecule that utilizes the mechanistic pathways of current second-generation androgen signaling inhibitors, while also introducing a distinct third mechanism – androgen receptor degradation. We are developing galeterone for the treatment of patients with metastatic castration resistant prostate cancer, or mCRPC.

We are conducting a pivotal Phase 3 clinical trial comparing galeterone to Xtandi® (enzalutamide) in approximately 148 treatment-naïve mCRPC patients whose prostate tumors express the AR-V7 splice variant. We refer to this clinical trial as ARMOR3-SV. We believe that the AR-V7 splice variant is the most common form of C-terminal loss, or the loss of the portion of the androgen receptor that contains the ligand-binding domain. C-terminal loss generally, and AR-V7 specifically, has been associated with poor responsiveness to commonly-used oral therapies for mCRPC. ARMOR3-SV is, to our knowledge, the first precision-medicine based pivotal clinical trial in prostate cancer. Selection of patients with AR-V7 is made using a clinical trial assay developed by our collaborator, Qiagen Manchester Limited, or Qiagen. We believe that the design of ARMOR3-SV is aligned with feedback that we obtained from the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency. We expect to complete enrollment in ARMOR3-SV by the end of 2016 and to have top-line data available from the study by mid-2017. We have been given fast track designation by the FDA for galeterone for the treatment of mCRPC.

As of December 31, 2015, galeterone had been administered to over 250 prostate cancer patients and healthy volunteers in clinical trials. In these trials, which included patients whose tumor cells did not express AR-V7, galeterone was well tolerated and clinically meaningful reductions in levels of prostate specific antigen or PSA, a biochemical marker used to evaluate prostate cancer patients for signs of response to therapy, were observed in prostate cancer patients. Therefore, and subject to the availability of resources, we anticipate expanding the clinical development of galeterone in other indications or patient populations.

We initially plan to conduct two additional open-label studies of galeterone in mCRPC patients who have shown resistance following treatment with either Xtandi or Zytiga® (abiraterone acetate). The first of these studies, which we anticipate initiating in the first half of 2016, is an expansion of an arm of our ongoing Phase 2 clinical trial of galeterone, referred to as ARMOR2, in mCRPC patients who have developed acquired resistance to Xtandi. The other study, which we also expect to initiate in the first half of 2016, is designed to evaluate galeterone in men whose mCRPC rapidly progressed after initial treatment with either Xtandi or Zytiga. We plan to evaluate all patients enrolled in this new Phase 2 clinical trial for the presence of AR-V7, but AR-V7 positive status is not a criterion for participation in this trial.

We have worldwide development and commercialization rights to galeterone. To maximize the value of these rights, we intend to build a urology- and oncology-focused specialty sales and marketing organization in the United States to support the commercialization of galeterone. We intend to commercialize galeterone outside the United States through collaborations with third parties.

Since our inception in March 2004, we have devoted substantially all of our resources to developing our product candidates, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. To date, we have financed our operations primarily through our initial public offering of our common stock, and prior to our initial public offering, through private placements of our redeemable convertible preferred stock and convertible promissory notes. In September 2014, we completed the initial public offering of our common stock through the issuance and sale of 6,480,000 shares of our common stock at a price to the public of $15.00 per share, resulting in net proceeds of $87.1 million after deducting underwriting discounts and commissions and offering expenses. In October 2014, we issued and sold an additional 540,000 shares of our common stock as a result of the partial exercise by the underwriters of their option to purchase additional shares of common stock at the public offering price of $15.00 per share, and received additional net proceeds of $7.5 million after deducting underwriting discounts and commissions.

We have never generated any revenue and have incurred net losses in each year since our inception. Our net loss was $45.1 million for the year ended December 31, 2015, $23.3 million for the year ended December 31, 2014 and $15.7 million for the year ended December 31, 2013. As of December 31, 2015, we had an accumulated deficit of $131.4 million. This deficit has resulted principally from costs incurred in connection with research and development activities, general and administrative costs associated with our operations and in-licensing our product candidates. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially if and as we:

- conduct ARMOR3-SV and other clinical trials and non-clinical studies to support the submission of a new drug application, or NDA, to the FDA for galeterone for AR-V7 positive mCRPC;
- develop a companion diagnostic test for use with galeterone in collaboration with Qiagen;
- conduct planned additional clinical trials of galeterone in mCRPC patients who have shown resistance following treatment with Xtandi or Zytiga;
- develop galeterone for the treatment of other indications and patient populations in prostate cancer;
- explore the use of galeterone for the treatment of other diseases that are associated with the androgen receptor signaling pathway;
- identify and develop compounds that are designed to disrupt androgen receptor signaling through enhanced androgen receptor degradation;
- enter into agreements with third parties to manufacture galeterone;
- establish a sales, marketing and distribution infrastructure to support the commercialization of galeterone in the United States;
- maintain, expand and protect our intellectual property portfolio;
- continue our other research and development efforts;
- acquire or in-license additional compounds or technologies; and
- operate as a public company.

Our ability to generate product revenue, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and eventual commercialization of galeterone and other product candidates that we may develop in the future. As a result, we will need additional financing to support our continuing operations until such time that we can generate significant revenue from product sales, if ever. We expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. We may be unable to raise capital when needed or on acceptable terms, which would force us to delay, limit, reduce or terminate our research and development programs or commercialization efforts. We will need to generate significant revenue to achieve profitability, and we may never do so.

As of December 31, 2015, we had cash and investments of $64.0 million. We expect that our existing cash and investments will only be sufficient to enable us to fund our planned operating expenses and capital expenditure requirements into the first half of 2017. We will need to obtain substantial additional funding in order to complete the development of, and to commercialize, galeterone for patients with AR-V7 positive mCRPC and in other indications and patient populations, submit an NDA to the FDA for galeterone, conduct other clinical trials of galeterone, and develop or commercialize any future product candidates. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce, terminate or eliminate our product development programs and our commercialization efforts. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for galeterone or other product candidates that we may develop in the future are successful and result in regulatory approval or license or collaboration agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties.

Operating Expenses

The majority of our operating expenses consist of research and development activities and general and administrative costs.

Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, include the following:

- third-party contract costs relating to research, formulation and manufacturing, preclinical studies and clinical trial activities;
- third-party contract costs relating to development of a companion diagnostic test for use with galeterone, including the AR-V7 clinical trial assay being used to identify eligible patients for ARMOR3-SV;
- personnel costs, including salaries, related benefits and stock-based compensation for personnel engaged in research and development functions;
- consulting fees paid to third parties;
- costs related to compliance with regulatory requirements;
- payments made under our third-party licensing agreements; and
- allocated facility-related costs.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, payments made under our licensing agreements or other internal costs to specific development programs or product candidates. These costs are included in unallocated research and development expenses in the tables below. See "Results of Operations — Comparison of the Years Ended December 31, 2015 and 2014" and "— Comparison of the Years Ended December 31, 2014 and 2013."

Research and development activities are central to our business. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development,

primarily due to the increased size and duration of later-stage clinical trials. To date, we have focused substantially all of our research and development efforts on the development of galeterone. We incurred total research and development expenses of $32.6 million for the year ended December 31, 2015, $14.6 million for the year ended December 31, 2014 and $12.2 million for the year ended December 31, 2013. We expect that our research and development expenses will continue to increase as we conduct ARMOR3-SV, other clinical trials and additional NDA-enabling activities for galeterone, and develop any future product candidates.

We are currently conducting ARMOR3-SV, our pivotal Phase 3 clinical trial of galeterone, and plan to expand our clinical development program for galeterone. We cannot determine with certainty the duration and completion costs of ARMOR3-SV or any future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical studies and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of our ongoing clinical trials as well as any additional clinical trials and other research and development activities that we may conduct;
- future clinical trial results;
- uncertainties in clinical trial design and patient enrollment rate;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in patient enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, including salaries, related benefits and stock-based compensation expense, of our executive, finance, business and corporate development and other administrative functions. General and administrative expenses also include professional fees for auditing, tax and legal services, including legal expenses to pursue protection of our intellectual property, pre-commercialization costs, insurance costs, travel expenses and allocated facility-related costs.

We expect that our general and administrative expenses will increase in future periods as we establish capabilities that would enable the potential commercialization of galeterone for the treatment of mCRPC and any future product candidates, and as a result of increased payroll, expanded infrastructure, increased insurance, consulting, legal, accounting and investor relations expenses associated with being a public company and costs incurred to seek collaborations with respect to galeterone and any other product candidates that we may develop in the future.

Interest and Other Income (Expense), net

Interest and other income (expense), net, consists of interest income and miscellaneous income and expense unrelated to our core operations. Interest income consists of interest earned on our cash and investments. Our interest income has not been significant due to low interest earned on invested balances.

Income Taxes

Since our inception in 2004, we have not recorded any U.S. federal or state income tax benefits for either the net losses we have incurred or our earned research and development tax credits, due to the uncertainty of realizing a benefit from those items in the future. As of December 31, 2015, we had federal and state net operating loss carryforwards of $27.9 million and $24.2 million respectively. Our federal and state net operating loss carryforwards begin to expire in 2024 and 2030, respectively. We also had federal and state research and development tax credit carryforwards of $1.0 million and $0.4 million, respectively, as of December 31, 2015, which begin to expire in 2025 and 2023, respectively. Our federal and state net operating loss carryforwards do not yet include the effect of research and development expenses of $96.1 million that we have capitalized for income tax purposes as of December 31, 2015.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We believe that the estimates, assumptions and judgments involved in the accounting policies described below may have the greatest potential impact on our financial statements and, therefore, consider these to be our critical accounting policies. Accordingly, we evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions. See also Note 2, *Summary of Significant Accounting Policies,* of the Notes to Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for information about these critical accounting policies, as well as a description of our other significant accounting policies.

Research and Development Expenses

Research and development costs are expensed as incurred. Included in research and development expenses are salaries, stock-based compensation and benefits of employees, third-party license fees and other operational costs related to the Company's research and development activities, including manufacturing expenses and external costs of outside vendors engaged to conduct both preclinical studies and clinical trials. We expense raw materials used to manufacture our drug substance when received.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel and outside vendors to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- clinical research organizations in connection with clinical trials;
- investigative sites or other providers in connection with clinical trials;
- Qiagen in connection with the development of the AR-V7 clinical trial assay and companion diagnostic test;
- vendors in connection with preclinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple clinical research organizations and investigative sites that manage and conduct clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. For the years ended December 31, 2015, 2014 and 2013, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Accounting for Stock-Based Compensation

We measure all stock options and other stock-based awards granted to employees and directors at the fair value on the date of the grant. The fair value of the awards is recognized as compensation expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The straight-line method of expense recognition is applied to all awards with service-only conditions, while the graded vesting method is applied to all grants with both service and performance conditions. For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of the unvested portion of the awards is re-measured using the then-current fair value of the award.

We classify stock-based compensation expense in our consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Prior to September 2014, we were a privately-held company and lacked company-specific historical and implied volatility information. Therefore, we estimated our expected volatility based on the historical volatility of our publicly traded peer companies. We expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price following our initial public offering. The expected term assumption is based on the "simplified method" for estimating the expected term for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to U.S. Treasury bond yields at or near the time of grant for time periods similar to the expected term of the award. The relevant data used to determine the value of the stock option grants on a weighted average basis is as follows:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.79%	1.83%	1.72%
Expected term (in years)	6.01	5.95	5.98
Expected volatility	74.2%	79.4%	79.7%
Expected dividend yield	0%	0%	0%

The assumptions used in determining the fair value of stock-based awards represent our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change

and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different in the future. We recognize compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, we considered our historical experience of actual forfeitures to estimate pre-vesting forfeitures for service-based awards. The impact of a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual forfeiture rate is materially different from our estimate, we may be required to record adjustments to stock-based compensation expense in future periods.

JOBS Act

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years from the date of our initial public offering. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an "emerging growth company," we elected not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision not to take advantage of the extended transition period is irrevocable. Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company", we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis), and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer's compensation to median employee compensation.

Results of Operations

Comparison of the Years Ended December 31, 2015 and 2014

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014:

	Year Ended December 31,		
	2015	2014	Change
	(in thousands)		
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	32,638	14,577	18,061
General and administrative	12,623	8,885	3,738
Total operating expenses	45,261	23,462	21,799
Loss from operations	(45,261)	(23,462)	(21,799)
Interest and other income (expense), net	174	166	8
Net loss	$ (45,087)	$ (23,296)	$(21,791)

Research and Development Expenses

	Year Ended December 31,		
	2015	2014	Change
	(in thousands)		
Galeterone for prostate cancer	$ 27,674	$ 10,970	$16,704
Other early-stage development programs and additional indications for galeterone	685	139	546
Unallocated research and development expenses	4,279	3,468	811
Total research and development expenses	$ 32,638	$ 14,577	$18,061

The increase in research and development expenses associated with our galeterone for prostate cancer program for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily due to increased costs of clinical trials of $10.4 million, costs associated with the development of our AR-V7 clinical trial assay and companion diagnostic test of $3.9 million, and increased manufacturing costs of $2.1 million. The increase in clinical trial costs was primarily related to the initiation of ARMOR3-SV during 2015, and costs associated with other clinical trials to support the submission of an NDA for galeterone. ARMOR3-SV costs included the purchase of Xtandi to be used in the trial for comparison against galeterone. Costs associated with the development of our AR-V7 clinical trial assay and companion diagnostic test included a fee paid for the exclusive right to have the circulating tumor cell enrichment technology used in the assay and companion diagnostic test. The increase in manufacturing costs was primarily due to a large purchase of raw materials during the year ended December 31, 2015 for use in the manufacture of registration lots and process validation activities required to support the submission of an NDA for galeterone. The increase in unallocated research and development expenses was primarily due to increased personnel related costs and facility costs as a result of increased headcount in our research and development function.

General and Administrative Expenses

	Year Ended December 31,		
	2015	2014	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$ 5,671	$ 4,022	$1,649
Professional and consultant fees	4,793	3,863	930
Facility related and other	2,159	1,000	1,159
Total general and administrative expenses	$ 12,623	$ 8,885	$3,738

The increase in personnel related costs for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily due to increased headcount in our general and administrative function and an increase in overall compensation. Personnel related costs also increased in 2015 due to an increase in stock-based compensation expense of $0.7 million related to additional employee stock options granted and a higher value of our common stock. Professional and consultant fees increased in 2015 compared to 2014 primarily due to an increase of $2.0 million in patent costs and other fees associated with operating as a public company and costs associated with pre-commercialization activities, partially offset by a $1.1 million fee incurred in 2014 in connection with strategic and financial advisory services that was not incurred in 2015. Facility related and other costs increased primarily due to increased insurance premiums, facility costs related to our new office lease and other costs related to our growth and operating as a public company.

Interest and Other Income (Expense), net

For the year ended December 31, 2015, interest and other income (expense), net consisted primarily of interest on investments. For the year ended December 31, 2014, interest and other income (expense), net consisted primarily of the collection of a loan receivable which had been fully reserved for in prior years.

Comparison of the Years Ended December 31, 2014 and 2013

The following table summarizes our results of operations for the years ended December 31, 2014 and 2013:

	Year Ended December 31,		
	2014	2013	Change
	(in thousands)		
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	14,577	12,201	2,376
General and administrative	8,885	3,548	5,337
Total operating expenses	23,462	15,749	7,713
Loss from operations	(23,462)	(15,749)	(7,713)
Interest and other income (expense), net	166	24	142
Net loss	$ (23,296)	$ (15,725)	$(7,571)

Research and Development Expenses

	Year Ended December 31,		
	2014	2013	Change
	(in thousands)		
Galeterone for prostate cancer	$ 10,970	$ 10,257	$ 713
Other early-stage development programs and additional indications for galeterone	139	40	99
Unallocated research and development expenses	3,468	1,904	1,564
Total research and development expenses	$ 14,577	$ 12,201	$2,376

The increase in research and development expenses associated with our galeterone for prostate cancer program for the year ended December 31, 2014 compared to the year ended December 31, 2013 was primarily due to increased costs of clinical trials of $3.0 million and an increase of $0.1 million in costs related to non-clinical studies to support our galeterone for prostate cancer program, partially offset by decreased manufacturing costs of $2.3 million. The increase in clinical trial costs was due to an increased number of patients and sites in our ARMOR2 trial in the year ended December 31, 2014 as compared to the year ended December 31, 2013. The decrease in manufacturing costs was due to higher costs incurred in 2013 to manufacture galeterone for use in our ARMOR2 trial and in anticipation of our planned pivotal Phase 3 clinical trial of galeterone, including a large purchase of raw materials in 2013. Manufacturing costs in 2013 also included costs related to the technology transfer of our manufacturing process to a new vendor. The increase in unallocated research and development expenses was due to increased personnel related costs, including stock-based compensation expense, as a result of increased headcount in our research and development function.

General and Administrative Expenses

	Year Ended December 31,		
	2014	2013	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$ 4,022	$ 1,731	$2,291
Professional and consultant fees	3,863	1,392	2,471
Facility related and other	1,000	425	575
Total general and administrative expenses	$ 8,885	$ 3,548	$5,337

The increase in personnel related costs for the year ended December 31, 2014 compared to the year ended December 31, 2013 was primarily due to stock-based compensation expense of $2.1 million compared to $0.2 million for the year ended December 31, 2013. The increase of $1.9 million in stock-based compensation expense was related to additional employee stock options and a higher value of our common stock, as well as $0.9 million recorded in the three months ended September 30, 2014 that was related to the vesting of a performance-based option grant upon the closing of our initial public offering in September 2014. Personnel related costs also increased as a result of increased headcount in our general and administrative function and an increase in overall compensation, partially offset by a decrease in personnel related costs due to severance paid to our former Chief Executive Officer in the year ended December 31, 2013. The increase in professional and consultant fees primarily consisted of a $1.1 million fee payable to a financial advisor upon the closing of our initial public offering in connection with strategic and financial advisory services unrelated to the offering and an increase in accounting, public relations and patent fees associated with ongoing business activities and our preparations to operate as a public company as well as consulting fees for an external market research study that was conducted in 2014. Facility related and other expenses increased primarily due to increased insurance costs of $0.2 million related to our being a public company, increased facility costs of $0.2 million to accommodate our additional employees and increased other taxes of $0.1 million.

Interest and Other Income (Expense), net

For the year ended December 31, 2014, interest and other income (expense), net consisted primarily of collection of a loan receivable from a former advisor, which had been fully reserved for in prior years.

Liquidity and Capital Resources

Since our inception in March 2004, we have not generated any revenue and have incurred recurring net losses. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may obtain from additional financings, research funding, collaborations, contract and grant revenue or other sources.

To date, we have funded our operations primarily through our initial public offering of our common stock, and prior to our initial public offering, private placements of our redeemable convertible preferred stock and convertible promissory notes. In September 2014, we completed the initial public offering of our common stock through the issuance and sale of 6,480,000 shares of our common stock at a price to the public of $15.00 per share, resulting in net proceeds of $87.1 million after deducting underwriting discounts and commissions and offering expenses. In October 2014, we issued and sold an additional 540,000 shares of our common stock as a result of the partial exercise by the underwriters of their option to purchase additional shares of common stock at the public offering price of $15.00 per share and received additional net proceeds of $7.5 million after deducting underwriting discounts and commissions.

Cash Flows

As of December 31, 2015, we had cash and cash equivalents of $24.0 million. We invest our cash equivalents in money market accounts in order to preserve principal.

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Cash used in operating activities	$ (41,236)	$ (21,121)	$(15,476)
Cash used in investing activities	(40,510)	(175)	(53)
Cash provided by financing activities	513	94,799	35,591
Net increase (decrease) in cash and cash equivalents	$ (81,233)	$ 73,503	$ 20,062

Operating activities. During the year ended December 31, 2015, cash used in operating activities consisted of our net loss of $45.1 million, partially offset by net non-cash charges of $2.8 million and by net cash provided by changes in our operating assets and liabilities of $1.0 million. Our net non-cash charges during the period consisted primarily of stock-based compensation expense. Cash provided by changes in our operating assets and liabilities consisted primarily of an increase in accounts payable and accrued expenses of $1.9 million, partially offset by an increase in prepaid expenses and other current assets of $1.0 million.

During the year ended December 31, 2014, cash used in operating activities was $21.1 million, resulting from our net loss of $23.3 million, partially offset by net non-cash charges of $2.0 million and by net cash provided by changes in our operating assets and liabilities of $0.2 million. Our net non-cash charges during the period consisted primarily of stock-based compensation expense of $2.1 million. Cash provided by changes in our operating assets and liabilities consisted primarily of a net increase in accounts payable and accrued expenses of $2.0 million, partially offset by an increase in prepaid expenses and other current assets of $1.8 million.

During the year ended December 31, 2013, cash used in operating activities was $15.5 million, resulting from our net loss of $15.7 million, partially offset by non-cash charges of $0.2 million. Our net non-cash charges during the year ended December 31, 2013 consisted primarily of stock-based compensation expense of $0.2 million.

Our prepaid expenses and other current assets and accounts payable and accrued expense balances have historically been affected by the volume of business and the timing of vendor invoicing and payments.

Investing activities. During the year ended December 31, 2015, net cash used in investing activities was primarily attributable to purchases of marketable securities of $39.9 million and purchases of property and equipment of $0.6 million primarily related to the purchase of lab equipment and computer equipment.

We used a small amount of cash during the years ended December 31, 2014 and 2013 related to purchases of property and equipment and to increase our restricted cash balance related to our corporate credit cards.

Financing activities. During the year ended December 31, 2015, net cash provided by financing activities was attributable to proceeds from the exercise of stock options and the repayment of notes receivable.

During the year ended December 31, 2014, net cash provided by financing activities was primarily due to proceeds, net of underwriting discounts and commissions, of $97.9 million from our initial public offering, partially offset by payments of $3.3 million of deferred offering costs related to our initial public offering that were paid during the period.

During the year ended December 31, 2013, net cash provided by financing activities was primarily due to net proceeds of $35.4 million from the sale and issuance of our Series E redeemable convertible preferred stock.

Capital Requirements

Galeterone is still in clinical development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- conduct ARMOR3-SV and other clinical trials and non-clinical studies to support the submission of an NDA to the FDA for galeterone for AR-V7 positive mCRPC;
- develop a companion diagnostic test for use with galeterone in collaboration with Qiagen;
- conduct planned additional clinical trials of galeterone in mCRPC patients who have shown resistance following treatment with Xtandi or Zytiga;
- develop galeterone for the treatment of other indications and patient populations in prostate cancer;
- identify and develop compounds that are designed to disrupt androgen receptor signaling through enhanced androgen receptor degradation;
- enter into agreements with third parties to manufacture galeterone;
- establish a sales, marketing and distribution infrastructure to support the commercialization of galeterone in the United States;
- maintain, expand and protect our intellectual property portfolio;
- continue our other research and development efforts;
- acquire or in-license additional compounds or technologies; and
- operate as a public company.

As of December 31, 2015, we had cash and investments of $64.0 million. We expect that our existing cash and investments will only be sufficient to enable us to fund our planned operating expenses and capital expenditure requirements into the first half of 2017. We will need to obtain substantial additional funding in order to complete the development of, and to commercialize, galeterone for patients with AR-V7 positive mCRPC and in other indications and patient populations, submit an NDA to the FDA for galeterone, conduct other clinical trials of galeterone, and develop or commercialize any future product candidates. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce, terminate or eliminate our product development programs and our commercialization efforts.

We have based this estimate on assumptions that may prove to be wrong, as we may use our available capital resources sooner than we currently expect or our clinical trials may take longer than we anticipate. Because of the numerous risks and uncertainties associated with the development of galeterone and because the extent to which we may enter into collaborations with third parties for development of galeterone is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of galeterone.

Our future capital requirements for galeterone will depend on many factors, including:

- the progress and results of ARMOR3-SV and our efforts to complete the clinical development of galeterone and submit an NDA to the FDA and marketing authorization applications to regulatory authorities outside of the United States;

- the progress and results of any additional clinical trials of galeterone that we decide to conduct in other indications and patient populations; including our planned trials in patients whose mCRPC has progressed after treatment with Xtandi and Zytiga;
- the timing and outcome of regulatory review of galeterone for the treatment of AR-V7 positive mCRPC and in any other indication or patient population, and of any other future product candidates;
- the progress and results of the development of a companion diagnostic test for use with galeterone in collaboration with Qiagen;
- the cost of commercialization activities, including product sales, marketing, manufacturing and distribution, for galeterone and our future product candidates for which we receive regulatory approval;
- the development of future product candidates, including our plans to seek to acquire or in-license additional compounds or technologies;
- revenue, if any, received from commercial sales of galeterone and any future product candidates, should any of our product candidates be approved by the FDA or a similar regulatory authority outside the United States;
- our ability to establish collaborations on favorable terms, if at all, particularly arrangements to develop, market and distribute galeterone and any future product candidates outside the United States; and
- the cost of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Until such time, if ever, that we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To this end, in October 2015, we filed and the SEC declared effective a shelf registration statement registering an aggregate of $150 million in various equity and debt securities. We have not issued or sold any securities under this registration statement. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that require liens to be placed on our property and include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute our common stockholders' ownership interest. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or current or future product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market galeterone that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2015:

	Payments Due By Period				
	Total	Less than 1 year	1-3 Years	3-5 Years	More Than 5 Years
			(in thousands)		
Operating lease commitments (1)	$1,883	$ 555	$ 1,328	$ —	$ —
Total (2) (3)	$1,883	$ 555	$ 1,328	$ —	$ —

(1) We lease our headquarters in Boston, Massachusetts under an operating lease through July 2018.

(2) We are party to license agreements with University of Maryland, Baltimore and the Johns Hopkins University and a collaboration agreement with Qiagen under which we are obligated to make future payments upon the achievement of certain contingent milestones or pay royalties upon selling a commercial product or sublicensing the licensed technology. We have not included these amounts in the table above as we cannot estimate or predict when, or if, these amounts will become due.

For further details regarding (1) and (2) above see *Commitments and Contingencies,* of the Notes to the Consolidated Financial Statements included elsewhere in this Annual Report on form 10-K.

(3) We enter into contracts in the normal course of business with contract research organizations for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Recently Issued Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board issued Accounting Standards Update 2014-15, "*Presentation of Financial Statements — Going Concern* (*Subtopic 205-40).*" The new guidance addresses management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. Management's evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. The standard will be effective for the first interim period within annual reporting periods beginning after December 15, 2016. Early adoption is permitted. This guidance relates to footnote disclosure only and the adoption will not impact our financial position, results of operations or liquidity.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Fluctuation Risk

Our cash and investments as of December 31, 2015 consisted of money market accounts, certificates of deposit and government bonds. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates. Because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial condition or results of operations.

ITEM 8. ***FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA***

Tokai Pharmaceuticals, Inc.

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of
Tokai Pharmaceuticals, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, of changes in redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Tokai Pharmaceuticals, Inc. and its subsidiary at December 31, 2015 and 2014, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2015 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 10, 2016

Tokai Pharmaceuticals, Inc.

Consolidated Balance Sheets

(In thousands, except share and per share data)

	December 31, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$ 24,023	$ 105,256
Marketable securities	39,934	—
Prepaid expenses and other current assets	3,213	2,255
Total current assets	67,170	107,511
Property and equipment, net	489	33
Restricted cash	270	200
Other assets	45	—
Total assets	$ 67,974	$ 107,744
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,208	$ 765
Accrued expenses	4,954	3,478
Total current liabilities	6,162	4,243
Other long term liabilities	88	—
Total liabilities	6,250	4,243
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 22,597,144 and 22,382,340 shares issued and outstanding at December 31, 2015 and December 31, 2014, respectively	23	22
Additional paid-in capital	193,194	189,830
Accumulated other comprehensive loss	(55)	—
Accumulated deficit	(131,438)	(86,351)
Total stockholders' equity	61,724	103,501
Total liabilities and stockholders' equity	$ 67,974	$ 107,744

The accompanying notes are an integral part of these consolidated financial statements.

Tokai Pharmaceuticals, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share data)

	Year Ended December 31,		
	2015	2014	2013
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	32,638	14,577	12,201
General and administrative	12,623	8,885	3,548
Total operating expenses	45,261	23,462	15,749
Loss from operations	(45,261)	(23,462)	(15,749)
Interest and other income (expense), net	174	166	24
Net loss	$ (45,087)	$ (23,296)	$ (15,725)
Accretion of redeemable convertible preferred stock to redemption value	—	—	(94)
Net loss attributable to common stockholders	$ (45,087)	$ (23,296)	$ (15,819)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.01)	$ (3.60)	$ (38.02)
Weighted average common shares outstanding, basic and diluted	22,484,343	6,469,289	416,037
Comprehensive loss:			
Net loss	$ (45,087)	$ (23,296)	$ (15,725)
Other comprehensive loss:			
Unrealized loss on marketable securities	(55)	—	—
Total other comprehensive loss	(55)	—	—
Total comprehensive loss	$ (45,142)	$ (23,296)	$ (15,725)

The accompanying notes are an integral part of these consolidated financial statements.

Tokai Pharmaceuticals, Inc.

Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

(In thousands, except share data)

	Series A, B-1, B-2, C, D-1, D-2, D-3 and E Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balances at December 31, 2012	98,693,750	$ 49,845	464,633	$ —	$ 7,429	$ —	$ (47,330)	$ (39,901)
Issuance of Series E redeemable convertible preferred stock, net of issuance costs of $94	56,892,391	35,406	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	157,804	—	215	—	—	215
Repurchase and forfeiture of unvested restricted stock	—	—	(129,145)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	238	—	—	238
Accretion of Series E redeemable convertible preferred stock to redemption value	—	94	—	—	(94)	—	—	(94)
Net loss	—	—	—	—	—	—	(15,725)	(15,725)
Balances at December 31, 2013	155,586,141	85,345	493,292	—	7,788	—	(63,055)	(55,267)
Issuance of common stock upon exercise of stock options	—	—	8,875	—	16	—	—	16
Stock-based compensation expense	—	—	—	—	2,108	—	—	2,108
Conversion of preferred stock to common stock	(155,586,141)	(85,345)	14,860,173	15	85,330	—	—	85,345
Issuance of common stock upon initial public offering	—	—	7,020,000	7	97,922	—	—	97,929
Issuance costs	—	—	—	—	(3,334)	—	—	(3,334)
Net loss	—	—	—	—	—	—	(23,296)	(23,296)
Balances at December 31, 2014	—	—	22,382,340	22	189,830	—	(86,351)	103,501
Issuance of common stock upon exercise of stock options	—	—	201,153	1	463	—	—	464
Issuance of common stock upon vesting of restricted stock units	—	—	13,651	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	2,901	—	—	2,901
Unrealized loss on marketable securities	—	—	—	—	—	(55)	—	(55)
Net loss	—	—	—	—	—	—	(45,087)	(45,087)
Balances at December 31, 2015	—	$ —	22,597,144	$ 23	$ 193,194	$ (55)	$ (131,438)	$ 61,724

The accompanying notes are an integral part of these consolidated financial statements.

Tokai Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(In thousands)

	Year ended December 31,		
	2015	2014	2013
Cash flows from operating activities:			
Net loss	$ (45,087)	$ (23,296)	$(15,725)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	2,901	2,108	238
Depreciation expense	109	21	10
Release of reserve for loan to former advisor	(49)	(158)	—
Premium on purchase of marketable securities	(186)	—	—
Amortization of premium on marketable securities	72	—	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(958)	(1,830)	(190)
Accounts payable	443	760	(759)
Accrued expenses	1,476	1,274	950
Other assets	(45)	—	—
Other long-term liabilities	88	—	—
Net cash used in operating activities	(41,236)	(21,121)	(15,476)
Cash flows from investing activities:			
Purchases of marketable securities	(39,875)	—	—
Purchases of property and equipment	(565)	(25)	(23)
Change in restricted cash	(70)	(150)	(30)
Net cash used in investing activities	(40,510)	(175)	(53)
Cash flows from financing activities:			
Repayment of notes receivable	49	158	—
Proceeds from exercise of common stock options	464	16	215
Proceeds from initial public offering, net of underwriting discounts and commissions	—	97,929	—
Payments of initial public offering costs	—	(3,304)	(30)
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	—	35,406
Net cash provided by financing activities	513	94,799	35,591
Net increase (decrease) in cash and cash equivalents	(81,233)	73,503	20,062
Cash and cash equivalents at beginning of period	105,256	31,753	11,691
Cash and cash equivalents at end of period	$ 24,023	$105,256	$ 31,753
Supplemental disclosure of non-cash investing and financing activities:			
Conversion of redeemable convertible preferred stock to common stock	$ —	$ (85,345)	$ —
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ —	$ 94

The accompanying notes are an integral part of these consolidated financial statements.

Tokai Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements
(amounts in thousands, except share and per share amounts)

1. Nature of the Business and Basis of Presentation

Tokai Pharmaceuticals, Inc. (the "Company") was incorporated on March 26, 2004 under the laws of the State of Delaware. The Company is a biopharmaceutical company focused on developing and commercializing innovative therapies for the treatment of prostate cancer and other hormonally-driven diseases. The Company's lead drug candidate, galeterone, is an oral small molecule that utilizes the mechanistic pathways of current second-generation androgen signaling inhibitors, while also introducing a distinct third mechanism – androgen receptor degradation. The Company is developing galeterone for the treatment of patients with metastatic castration resistant prostate cancer ("mCRPC"). Since its inception, the Company has devoted substantially all of its efforts to research and development, in-licensing technology and raising capital.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. Galeterone, which is currently under development, and any product candidates that the Company may seek to develop in the future, will require significant additional research and development efforts, including extensive preclinical and clinical testing, and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure, and extensive compliance capabilities.

There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees, consultants and contracted service providers.

On September 22, 2014, the Company completed an initial public offering ("IPO") of its common stock through the issuance and sale of 6,480,000 shares of common stock at a price to the public of $15.00 per share, resulting in net proceeds of $87,062 after deducting underwriting discounts and commissions and offering expenses. Upon the closing of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock automatically converted into 14,860,173 shares of the Company's common stock. On October 9, 2014, the Company issued and sold an additional 540,000 shares of its common stock at the public offering price of $15.00 per share as a result of the partial exercise by the underwriters of their option to purchase additional shares of common stock, resulting in additional net proceeds to the Company of $7,533 after deducting underwriting discounts and commissions.

The Company's consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and satisfaction of liabilities in the ordinary course of business. The Company has incurred losses and negative cash flows from operations since inception. As of December 31, 2015, the Company had an accumulated deficit of $131,438 and had cash and investments of $63,957. The Company believes its cash and investments balance as of December 31, 2015 will only be sufficient to enable it to fund planned operating expenses and capital expenditure requirements into the first half of 2017. The Company will need to obtain substantial additional funding in order to complete the development of, and to commercialize, galeterone for patients with AR-V7 positive mCRPC and in other indications and patient populations, submit an NDA to the FDA for galeterone, conduct other clinical trials of galeterone, and develop or commercialize any future product candidates. If the Company is unable to raise capital when needed or on acceptable terms, it may be forced to delay, reduce, terminate or eliminate its product development programs and commercialization

efforts. The Company's ability to generate product revenue and operating cash flow will depend heavily on the successful development and eventual commercialization of galeterone and other product candidates that it may develop in the future.

The accompanying consolidated financial statements and footnotes include Diotima Pharmaceuticals, Inc. ("Diotima"), a variable interest entity in which the Company had a variable financial interest and was the primary beneficiary but had no ownership interest. In 2010, the Company formed and incorporated Diotima. Diotima operated as a stand-alone company with limited activity through April 2014. In early 2014, the license agreements relating to the Diotima compounds were terminated. Additionally, in April 2014, the board of directors and stockholders of Diotima approved the dissolution of Diotima, and Diotima was dissolved. All significant intercompany balances and transactions between the Company and Diotima have been eliminated in consolidation. Expenses incurred by Diotima for the years ended December 31, 2014 and 2013 were $8 and $60, respectively.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. Generally Accepted Accounting Principles requires management to make estimates, assumptions and judgments that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting periods. Significant estimates, assumptions and judgments reflected in these consolidated financial statements include, but are not limited to, the accrual of research and development expenses and the valuation of stock-based awards. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of ninety days or less at date of purchase to be cash equivalents. Cash equivalents, which consist of money market accounts, are stated at fair value.

Marketable Securities

The Company's marketable securities are classified as available-for-sale and are carried at fair value with the unrealized gains and losses reported as a component of accumulated other comprehensive loss in stockholders' equity (deficit). Realized gains and losses and declines in value judged to be other than temporary are included as a component of interest and other income (expense), net based on the specific identification method. The Company has classified its marketable securities with maturities beyond one year as short-term, based on their highly liquid nature and because such marketable securities are available for current operations.

Concentration of Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and marketable securities. The Company has all cash and cash equivalents and marketable securities' balances at two accredited financial institutions, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of

manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

The Company is dependent on Qiagen Manchester Limited ("Qiagen") to develop and commercialize a companion diagnostic test for use with galeterone to identify mCRPC patients with the AR-V7 splice variant. If Qiagen is unable to successfully develop and commercialize the companion diagnostic test, the development, approval and commercialization of galeterone could be adversely affected.

Fair Value Measurements

Certain assets and liabilities are carried at fair value. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices) such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method based upon estimated useful life as follows:

	Years
Lab equipment	3
Computer equipment	3
Furniture and fixtures	5
Leasehold improvements	Shorter of life of lease or estimated useful life

Upon retirement or sale of property and equipment, the cost and related accumulated depreciation of such property and equipment disposed of are removed from the accounts and any resulting gain or loss is included in loss from operations.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived

asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

Research and Development Costs

Research and development costs are expensed as incurred. Included in research and development expenses are salaries, stock-based compensation and benefits of employees, third-party license fees and other operational costs related to the Company's research and development activities, including manufacturing expenses and external costs of outside vendors engaged to conduct both preclinical studies and clinical trials. The Company expenses raw materials used to manufacture its drug substance when received.

As part of the process of preparing consolidated financial statements, the Company is required to estimate its accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with company personnel and outside vendors to identify services that have been performed on the Company's behalf and estimating the level of service performed and the associated costs incurred for the services when the Company has not yet been invoiced or otherwise notified of the actual costs. The majority of the Company's service providers invoice in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. The Company makes estimates of its accrued expenses as of each balance sheet date in its consolidated financial statements based on facts and circumstances known to the Company at that time. Examples of estimated accrued research and development expenses include fees paid to:

- clinical research organizations in connection with clinical trials;
- investigative sites or other providers in connection with clinical trials;
- Qiagen in connection with the development of the AR-V7 clinical trial assay and companion diagnostic test;
- vendors in connection with preclinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

The Company bases its expenses related to clinical trials on its estimates of the services received and efforts expended pursuant to contracts with multiple clinical research organizations and investigative sites that manage and conduct clinical trials on the Company's behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, the Company estimates the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from its estimate, the Company adjusts the accrual or amount of prepaid expense accordingly. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting amounts that are too high or too low in any particular period. For the years ended December 31, 2015, 2014 and 2013, the Company has not made any material adjustments to its prior estimates of accrued research and development expenses.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees and directors at the fair value on the date of the grant using the Black-Scholes option-pricing model. The fair value of the awards is recognized as expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The straight-line method of expense recognition is applied to all awards with service-only conditions, while the graded vesting method is applied to all grants with both service and performance conditions. For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of the unvested portion of the awards is re-measured using the then-current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The Company recognizes compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, the Company has considered its historical experience to estimate pre-vesting forfeitures for service-based awards. The impact of a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual forfeiture rate is materially different from the Company's estimate, the Company may be required to record adjustments to stock-based compensation expense in future periods.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in its consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than- not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

As of December 31, 2015, the Company has early adopted Accounting Standards Update 2015-17, *Balance Sheet Classification of Deferred Taxes*, issued by the Financial Accounting Standards Board (the "FASB") in November 2015, which simplifies the presentation of deferred income taxes by eliminating the need for entities to separate deferred income tax liabilities and assets into current and noncurrent amounts in a classified statement of financial position. The Company adopted this guidance retrospectively to all periods presented. As the Company had no current deferred tax assets or current tax liabilities on its consolidated balance sheet, the adoption of this guidance had no impact on the Company's financial statements.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on developing novel proprietary therapies for the treatment of prostate cancer and other hormonally-driven diseases. No revenue has been generated since inception. The Company holds tangible assets with a net book value of $175 in laboratories located outside of the United States.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the year ended December 31, 2015, the Company's only element of other comprehensive loss was unrealized loss on marketable securities. For the years ended December 31, 2014 and 2013, there was no difference between net loss and comprehensive loss.

Net Income (Loss) Per Share

In September 2014, upon the closing of the IPO, all of the outstanding shares of the Company's redeemable convertible preferred stock automatically converted into 14,860,173 shares of the Company's common stock. Prior to this conversion, the Company followed the two-class method when computing net income (loss) per share as the Company had issued shares that met the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. The Company's redeemable convertible preferred stock contractually entitled the holders of such shares to participate in dividends, but did not contractually require the holders of such shares to participate in losses of the Company. Accordingly, the two-class method did not apply for periods in which the Company reported a net loss or a net loss attributable to common stockholders resulting from dividends or accretion related to its redeemable convertible preferred stock.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of common shares, including potential dilutive common shares assuming the dilutive effect of outstanding stock options and unvested restricted common shares, as determined using the treasury stock method. For periods in which the Company has reported net losses, diluted net loss per common share attributable to common stockholders is the same as basic net loss per common share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

The following common stock equivalents outstanding as of December 31, 2015, 2014 and 2013 were excluded from the computation of diluted net loss per share for the years ended December 31, 2015, 2014 and 2013, because they had an anti-dilutive impact:

	December 31,		
	2015	2014	2013
Stock options to purchase common stock	2,861,011	2,146,927	1,124,116
Restricted common stock units	40,953	54,604	—
Redeemable convertible preferred stock (as converted to common stock)	—	—	14,860,173
	2,901,964	2,201,531	15,984,289

Recently Issued Accounting Pronouncements

In August 2014, the FASB issued Accounting Standards Update 2014-15, *Presentation of Financial Statements — Going Concern* (*Subtopic 205-40).* The new guidance addresses management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. Management's evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. The standard will be effective for the first interim period within annual reporting periods beginning after December 15, 2016. Early adoption is permitted. This guidance relates to footnote disclosure only and the adoption will not impact the Company's financial position, results of operations or liquidity.

3. Marketable Securities and Fair Value Measurements

As of December 31, 2015, marketable securities by security type consisted of:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Certificates of Deposit (due within one year)	$ 13,709	$ —	$ —	$ 13,709
Certificates of Deposit (due after one year through two years)	1,178	—	—	1,178
United States Treasury Notes (due within one year)	22,596	—	(47)	22,549
United States Treasury Notes (due after one year through two years)	2,506	—	(8)	2,498
Total	$ 39,989	$ —	$ (55)	$ 39,934

The Company did not have marketable securities as of December 31, 2014.

The following tables present the Company's fair value hierarchy for its cash equivalents and marketable securities, which are measured at fair value on a recurring basis as of December 31, 2015 and 2014:

	Fair Value Measurements at December 31, 2015 Using			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money Market Instruments	$ —	$ 18,361	$ —	$ 18,361
Marketable securities:				
Certificates of Deposit	—	14,887	—	14,887
United States Treasury Notes	—	25,047	—	25,047
Total	$ —	$ 58,295	$ —	$ 58,295

	Fair Value Measurements at December 31, 2014 Using			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money Market Instruments	$ —	$ 91,316	$ —	$ 91,316
Total	$ —	$ 91,316	$ —	$ 91,316

The carrying values of accounts payable and accrued expenses approximate their fair value due to the short-term nature of these liabilities.

4. Property and Equipment, net

Property and equipment, net consisted of the following as of December 31, 2015 and 2014:

	December 31,	
	2015	2014
Lab equipment	$ 322	$—
Computer equipment	243	91
Leasehold improvements	66	—
Furniture and fixtures	23	—
	654	91
Less: Accumulated depreciation	(165)	(58)
	$ 489	$ 33

Depreciation expense was $109, $21 and $10 for the years ended December 31, 2015, 2014 and 2013, respectively.

5. Accrued Expenses

Accrued expenses consisted of the following as of December 31, 2015 and 2014:

	December 31,	
	2015	2014
Accrued research and development expenses	$3,188	$1,853
Accrued payroll and related expenses	900	963
Accrued professional fees	699	497
Accrued other	167	165
	$4,954	$3,478

6. Redeemable Convertible Preferred Stock

Prior to the completion of its IPO in September 2014 (Note 7), the Company had outstanding Series A, Series B-1, Series B-2, Series C, Series D-1, Series D-2, Series D-3 and Series E redeemable convertible preferred stock (collectively, the "Redeemable Preferred Stock"). The Company classified the Redeemable Preferred Stock outside of stockholders' equity (deficit) because the shares contained redemption features that were not solely within the Company's control. In connection with the closing of the Company's IPO, all of the Company's outstanding Redeemable Preferred Stock automatically converted into common stock on a 10.47-for-1 basis. No Redeemable Preferred Stock was outstanding as of December 31, 2014 or 2015.

In May and October 2013, the Company issued an aggregate of 56,892,391 shares of Series E redeemable convertible preferred stock to existing and new investors at $0.62398475 per share for gross proceeds of $35,500. The Company incurred issuance costs of $94 in connection with the sale and issuance of these shares of Series E redeemable convertible preferred stock which were immediately accreted to the carrying value of the Series E redeemable convertible preferred stock.

7. Common Stock

On August 29, 2014, the Company effected a 1-for-10.47 reverse stock split of its issued and outstanding shares of common stock. Accordingly, all share and per share amounts for all periods presented in these consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split.

On September 22, 2014, the Company completed an IPO of its common stock through the issuance and sale of 6,480,000 shares of common stock at a price to the public of $15.00 per share, resulting in net proceeds of $87,062 after deducting underwriting discounts and commissions and offering expenses. Upon the closing of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock automatically converted into 14,860,173 shares of the Company's common stock. On October 9, 2014, the Company issued and sold an additional 540,000 shares of its common stock at the public offering price of $15.00 per share as a result of the partial exercise by the underwriters of their option to purchase additional shares of common stock, resulting in additional net proceeds to the Company of $7,533 after deducting underwriting discounts and commissions.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are not entitled to receive dividends, unless declared by the board of directors.

8. Stock-Based Awards

The Company's 2014 Stock Incentive Plan (the "2014 Plan") permits the Company to make grants of incentive stock options, non-statutory stock options, restricted stock, restricted stock units, stock appreciation rights and other stock-based awards to the Company's employees, officers, directors, consultants and advisors; however, incentive stock options may only be granted to the Company's employees. The number of shares initially reserved for issuance under the 2014 Plan was 1,745,413 shares of common stock and may be increased by the number of shares under the 2007 Stock Incentive Plan (the "2007 Plan") that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company. The number of shares of common stock that may be issued under the plan is also subject to an annual increase on the first day of each fiscal year equal to the lesser of (i) 1,800,000 shares of the Company's common stock, (ii) 4% of the number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year or (iii) an amount determined by the Company's board of directors. As of December 31, 2015, 1,156,154 shares remained available for issuance under the 2014 Plan. The number of authorized shares reserved for issuance under the 2014 Plan was increased by 903,885 shares effective as of January 1, 2016.

As required by the 2007 Plan and 2014 Plan, the exercise price for stock options granted is not to be less than the fair value of common stock as of the date of grant. The Company bases fair value of common stock on the quoted market price. Prior to the IPO, the value of common stock was determined by the Company's board of directors by taking into consideration its most recently available valuation of common stock performed by management and the board of directors as well as additional factors which might have changed since the date of the most recent contemporaneous valuation through the date of grant.

During the years ended December 31, 2015, 2014 and 2013, the Company granted options to purchase 996,845, 1,039,155 and 786,537 shares of common stock, respectively, to certain employees, consultants and directors. The vesting of most of these awards is time-based and the restrictions typically lapse over three to four years.

2014 Employee Stock Purchase Plan

Under the 2014 Employee Stock Purchase Plan (the "ESPP"), an aggregate of 225,000 shares of the Company's common stock are reserved for issuance. The number of shares of the Company's common stock reserved for issuance under the ESPP will automatically increase on the first day of each fiscal year equal to the lesser of (1) 450,000 shares of the Company's common stock, (2) 1% of the total number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year and (3) an amount determined by the Company's board of directors. No offering periods have commenced under the ESPP and the number of shares reserved for issuance under the ESPP have not increased.

Stock Option Valuation

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Prior to its IPO, the Company was a private company and lacked company-specific historical and implied volatility information. Therefore, the Company estimated its expected stock volatility based on the historical volatility of a publicly traded group of peer companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The following table sets forth the assumptions that the Company used to determine the fair value of the stock options granted, presented on a weighted average basis:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.79%	1.83%	1.72%
Expected term (in years)	6.01	5.95	5.98
Expected volatility	74.2%	79.4%	79.7%
Expected dividend yield	0%	0%	0%

The following table summarizes the Company's stock option activity from January 1, 2015 through December 31, 2015:

	Shares Issuable Under Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2014	2,146,927	$ 5.54	8.6	$ 19,802
Granted	996,845	10.60		
Exercised	(201,153)	2.31		
Forfeited	(81,608)	4.27		
Outstanding as of December 31, 2015	2,861,011	$ 7.57	8.3	$ 7,906
Options vested and expected to vest as of December 31, 2015	2,822,786	$ 7.52	8.2	$ 7,896
Options exercisable as of December 31, 2015	1,199,676	$ 4.10	7.0	$ 6,455

The aggregate intrinsic value was calculated based on the positive differences between the market value of the Company's common stock on December 31, 2015 and 2014, of $8.72 and $14.74 per share, respectively, and the exercise prices of the options.

The weighted average grant date fair value of stock options granted was $6.94, $6.70 and $1.17 per share for the years ended December 31, 2015, 2014 and 2013, respectively.

The total intrinsic value of stock options exercised was $2,236, $35 and $33 for the years ended December 31, 2015, 2014 and 2013, respectively.

Restricted Common Stock Units

The 2014 Plan provides for the award of restricted common stock units. The Company has granted restricted common stock units with time-based vesting conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award.

The table below summarizes the Company's restricted stock unit activity from January 1, 2015 through December 31, 2015:

	Shares	Weighted Average Grant Date Fair Value
Unvested restricted common stock units as of December 31, 2014	54,604	$ 15.00
Issued	—	—
Vested	(13,651)	15.00
Forfeited	—	—
Unvested restricted common stock units as of December 31, 2015	40,953	$ 15.00

During 2014, the Company granted 54,604 restricted stock units with a fair value of $15.00 per share that are subject to time-based vesting conditions that lapse over four years. Upon vesting, the restricted stock units entitle the holder to one share of common stock for each restricted stock unit. All restricted stock units currently granted have been classified as equity instruments as their terms require settlement in shares. Restricted stock units with time-based vesting conditions are valued on the grant date using the grant date market price of the underlying shares. As of December 31, 2015, the Company estimates that all shares of restricted stock units with an intrinsic value of $357 and a weighted average remaining contractual term of 2.67 years will ultimately vest. The Company did not grant restricted stock units in 2015 or 2013.

Stock-based Compensation

The Company recorded stock-based compensation expense related to stock options and restricted common stock units in the following expense categories of its statements of operations:

	Year Ended December 31,		
	2015	2014	2013
Research and development	$ 634	$ 552	$ 91
General and administrative	2,267	1,556	147
	$2,901	$2,108	$238

Stock-based compensation expense for the year ended December 31, 2014 includes $880 of stock-based compensation expense related to a performance-based option grant which vested during 2014.

As of December 31, 2015, the Company had an aggregate of $10,738 of unrecognized stock-based compensation expense, which it expects to recognize over a weighted average period of 3.06 years.

9. Commitments and Contingencies

Leases

In February 2015, the Company entered into a sublease with a Massachusetts limited liability company (the "sublandlord") for 15,981 square feet of office space in Boston, Massachusetts. The sublease is subject and

subordinate to a prime lease, dated October 5, 2010, between the sublandlord and the prime landlord. The term of the sublease commenced on April 1, 2015 and expires on December 31, 2016. If the term of the prime lease is terminated for any reason prior to the expiration or earlier termination of the sublease, the sublease will terminate immediately and the Company will have no recourse against the sublandlord for such termination. In June 2015, the Company entered into a lease for the existing space with the prime landlord (the "landlord") which effectively extends the term of the lease of the existing space until July 31, 2018. Payment escalations specified in the lease agreements are accrued such that rent expense per square foot is recognized on a straight-line basis over the terms of occupancy.

Prior to April 2015, the Company leased office space in Cambridge, Massachusetts, and obtained certain office-related services on a month-to-month basis under a 30-day cancelable operating service agreement. The Company recorded exit costs of $133 included in rent expense during the year ended December 31, 2015 in connection with the termination of the Cambridge lease.

During the years ended December 31, 2015, 2014 and 2013, the Company recognized $835, $520 and $366, respectively, of rental expense related to office space.

As of December 31, 2015, future minimum lease payments under noncancelable office leases are as follows:

2016	$ 555
2017	839
2018	489
	$1,883

Restricted Cash and Letters of Credit

As of December 31, 2015 and 2014, the Company held a money market account to collateralize a credit card account with its bank of $200, which was classified as restricted cash on the consolidated balance sheet as of December 31, 2015 and 2014. In connection with the new office lease entered into in 2015, the Company was required to maintain a letter of credit totaling $70 for the benefit of the landlord of the new lease. The landlord can draw against the letter of credit in the event of default by the Company. The Company holds $70 in a money market account to collateralize the letter of credit, which amount is also included in restricted cash on the balance sheet as of December 31, 2015.

Intellectual Property Licenses

The Company has a master license agreement with the University of Maryland, Baltimore ("UMB"). Pursuant to the license agreement, UMB granted an exclusive, worldwide license, with the right to sublicense, under certain patents and patent applications to make, have made, use, sell, offer to sell and import certain anti-androgen steroids, including galeterone, for the prevention, diagnosis, treatment or control of any human or animal disease. In addition, UMB granted the Company a first option to receive an exclusive license to UMB's rights in certain improvements to the licensed products. The Company has exercised its option and acquired exclusive rights to licensed improvements under three amendments to the license agreement. The Company is obligated to pay UMB an annual maintenance fee of $10 each year until the first commercial sale of a product developed using the licensed technology. The Company is also obligated to make an additional $50 milestone payment to UMB for each additional investigational new drug application filed for a licensed product and a $100 milestone payment upon the approval by the U.S. Food and Drug Administration of each new drug application ("NDA") for a licensed product. Because none of these milestones have been achieved as of December 31, 2015, no liabilities for such milestone payments have been recorded in the Company's consolidated financial statements.

The Company must also pay UMB a low-single digit percentage royalty on aggregate worldwide net sales of licensed products, including sales by sublicensees, on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last-to-expire applicable licensed patent or ten years after first commercial sale of the applicable licensed product, in each case in the applicable country. The royalty obligations are subject to specified reductions in the event that additional licenses need to be obtained from third parties or in the event of specified competition from third-party products licensed by UMB. Minimum annual royalty payments to UMB are $50 beginning in the year following the year in which the first commercial sale occurs. The Company must also pay UMB 10% of all non-royalty sublicense income received from sublicensees. Finally, the Company is responsible for all patent expenses related to the prosecution and maintenance of the licensed patents. As of December 31, 2015, the Company has not yet developed a commercial product using the licensed technologies, nor has it entered into any sublicense agreements for the technologies.

In January 2015, the Company entered into an exclusive license agreement with The Johns Hopkins University ("Johns Hopkins") pursuant to which Johns Hopkins granted the Company an exclusive, worldwide license under certain patents and patent applications, and a non-exclusive license under certain know-how, in each case with the right to sublicense, to make, have made, use, sell, offer to sell and import certain assays to identify androgen receptor variants for use as a companion diagnostic with galeterone. In addition, Johns Hopkins granted the Company an option to negotiate an exclusive license to Johns Hopkins's rights in certain improvements to the licensed intellectual property.

Under the terms of the license agreement, the Company is obligated to diligently develop, manufacture and sell licensed products. The Company is also obligated to use commercially reasonable efforts to achieve specified milestone events by specified dates. Unless the license agreement with Johns Hopkins is terminated earlier as provided below, the license from Johns Hopkins expires on a country-by-country basis as of the later of the expiration date of the last to expire of the claims of the patent rights licensed under the agreement in such country or ten years after the first commercial sale of a licensed product in such country. Johns Hopkins may terminate the agreement if the Company fails to achieve such milestone events and does not cure such failure within a specified termination notice period. Johns Hopkins may also terminate the agreement upon a material breach by the Company under the agreement if the Company does not cure such breach within a specified notice period or upon the Company's bankruptcy or insolvency. The Company may terminate the agreement at any time upon 90 days' notice.

In consideration for the rights granted to the Company under the license agreement, the Company made an upfront payment to Johns Hopkins of $75 following the execution of the license agreement, which was recognized as research and development expense during the year ended December 31, 2015. The Company is obligated to pay Johns Hopkins an annual minimum royalty of up to $30 and to make milestone payments to Johns Hopkins upon the achievement of specified technical and commercial milestones. If all such milestones were achieved, the total milestone payments owed to Johns Hopkins would equal $700 in the aggregate. During the year ended December 31, 2015, the Company expensed $50 related to the achievement of two of these milestones. The Company has not achieved any other milestones and therefore no additional liabilities for such milestone payments have been recorded in the Company's consolidated financial statements.

The Company must also pay Johns Hopkins single digit percentage royalties on aggregate worldwide net sales of licensed products (but not galeterone), including sales by sublicensees, on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last-to-expire applicable licensed patent or ten years after first commercial sale of the applicable licensed product, in each case in the applicable country. These royalty obligations are subject to specified reductions in the event that additional licenses from third parties are required. The Company must also pay Johns Hopkins 20% of all non-royalty sublicense income received from sublicensees and reimburse Johns Hopkins for patent costs. As of December 31, 2015, the Company has not yet developed a commercial product using the licensed technologies.

Companion Diagnostic Development Agreement

In March 2015, the Company entered into a project work plan with Qiagen under a Master Collaboration Agreement, dated January 12, 2015, between the Company and Qiagen (together with the project work plan, the "CDx Agreement"). Pursuant to the CDx Agreement, Qiagen has agreed to develop and commercialize a companion diagnostic test for use with galeterone to identify mCRPC patients with the AR-V7 splice variant. Qiagen has also developed under the CDx Agreement a clinical trial assay for use in our pivotal Phase 3 clinical trial of galeterone in order to identify mCRPC patients whose tumor cells express AR-V7.

Under the CDx Agreement, Qiagen is responsible for developing, and obtaining and maintaining regulatory approvals for the companion diagnostic test in the United States, the European Union, Canada, Australia and such other countries as the parties may agree. In addition, Qiagen has agreed to use commercially reasonable and diligent efforts to manufacture the companion diagnostic test and to make the companion diagnostic test commercially available in those countries in which the Company has obtained regulatory approval for, and has valid patent claims covering, galeterone. Qiagen will be responsible for commercializing the companion diagnostic in each such country. If Qiagen elects not to commercialize the companion diagnostic test itself in any such country, for so long as there are valid patent claims covering galeterone in such country, Qiagen has agreed to procure alternative distribution channels or otherwise supply the companion diagnostic test to the Company in order for the Company to market galeterone in combination with the companion diagnostic test. Upon the request of the Company, the parties have also agreed to negotiate in good faith to expand the scope of the projects under the Agreement to, among other things, provide for the development and commercialization of the companion diagnostic test for use with galeterone in Japan.

Subject to the terms of the CDx Agreement, the Company paid Qiagen a fee for the exclusive right to have the circulating tumor cell enrichment technology used in the development of the companion diagnostic test, which was recognized as research and development expense during the year ended December 31, 2015. The Company will also pay Qiagen fees for the development of the AR-V7 clinical trial assay and a contingent milestone payment of $1,000 upon Qiagen obtaining pre-market approval of the companion diagnostic test. Furthermore, the Company will reimburse Qiagen for certain direct out-of-pocket costs incurred by Qiagen, including for sample material. These amounts are subject to adjustment if the parties determine that changes in the scope of the development program are required. Following commercialization, the Company will have no further payment obligations to Qiagen under the Agreement. The Company will not, however, receive any revenues from future sales, if any, of the companion diagnostic test.

The CDx Agreement expires on the later to occur of (i) the fifth anniversary of regulatory approval of the companion diagnostic test and (ii) the expiration of Qiagen's commercialization obligations under the CDx Agreement. The Company is permitted to terminate the CDx Agreement for convenience upon 180 days' written notice to Qiagen. Either party may terminate the CDx Agreement upon 60 days' written notice to the other party based on uncured material breaches by the other party and may terminate the CDx Agreement immediately based on the bankruptcy or insolvency of the other party.

Advisor Agreement

The Company paid a financial advisor $1,053 upon the closing of its IPO in connection with strategic and financial advisory services unrelated to the offering. The Company recorded this amount as general and administrative expense in its consolidated statement of operations and comprehensive loss for the year ended December 31, 2014.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third

parties. In addition, the Company has entered into indemnification agreements with each of its directors and executive officers, which provide, among other things, that the Company will indemnify such directors and executive officers to the fullest extent permitted by law for claims arising in his or her capacity as a director or officer. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of the indemnification agreements described above. In addition, the Company maintains directors and officers insurance coverage. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2015.

10. Income Taxes

During the years ended December 31, 2015, 2014 and 2013, the Company recorded no income tax benefits for the net operating losses incurred in each year, due to its uncertainty of realizing a benefit from those items.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2015	2014	2013
Federal statutory income tax rate	(34.0)%	(34.0)%	(34.0)%
Federal research and development tax credit	(0.5)	(0.9)	(0.7)
State taxes, net of federal benefit	(5.3)	(4.5)	(5.6)
Stock-based compensation expense	0.4	1.1	0.4
Other	0.1	0.2	0.1
Increase in deferred tax asset valuation allowance	39.3	38.1	39.8
Effective income tax rate	0.0%	0.0%	0.0%

Net deferred tax assets as of December 31, 2015 and 2014 consisted of the following:

	December 31,	
	2015	2014
Deferred tax assets:		
Capitalized research and development expenses	$ 37,765	$ 24,945
Net operating loss carryforwards	10,224	6,292
Stock-based compensation	1,371	612
Research and development tax credit carryforwards	1,273	1,008
Accrued expenses	339	414
Other	56	1
Total gross deferred tax assets	51,028	33,272
Valuation allowance	(51,028)	(33,272)
Net deferred tax assets	$ —	$ —

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2015, 2014 and 2013 related primarily to the increase in net operating loss carryforwards, capitalized research and development expenses and research and development tax credit carryforwards and were as follows:

	Year Ended December 31,		
	2015	2014	2013
Valuation allowance as of beginning of year	$33,272	$24,402	$18,138
Decreases recorded as benefit to income tax provision	—	—	—
Increases recorded to income tax provision	17,756	8,870	6,264
Valuation allowance as of end of year	$51,028	$33,272	$24,402

As of December 31, 2015, the Company had net operating loss carryforwards for federal and state income tax purposes of $27,900 and $24,200, respectively, which begin to expire in 2024 and 2030, respectively. As of December 31, 2015, the federal and state net operating loss carryforwards include $1,400 of deductions for stock option compensation for which the associated tax benefit will be credited to additional paid-in capital when realized. This amount is accounted for separately and is not included in the Company's deferred tax assets. As of December 31, 2015, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $1,040 and $353, respectively, which begin to expire in 2025 and 2023, respectively. Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code") due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. The Company has not conducted a formal study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382 of the Code, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards may be subject to an annual limitation under Section 382 of the Code, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2015 and 2014. Management reevaluates the positive and negative evidence at each reporting period.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2015 or 2014.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending income tax examinations. The Company's tax years are still open under statute from 2012 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

11. 401(k) Plan

The Company has a 401(k) plan available for participating employees who meet certain eligibility requirements. Eligible employees may defer a portion of their salary as defined by the plan. Company contributions to the plan may be made at the discretion of the Board of Directors. To date, the Company has not made any contributions to the plan. Effective January 1, 2016, the Company has elected to make matching contributions for the plan year ending December 31, 2016 at a rate of 100% of each employee's contribution up to a maximum matching contribution of 3% of the employee's compensation and at a rate of 50% of each employee's contribution in excess of 3% up to a maximum of 5% of the employee's compensation.

12. Related Party Transactions

The Company had an outstanding loan to a former advisor comprised of unpaid principal and interest in the amount of $220 that was deemed uncollectable and as a result, was fully reserved for in 2007. In 2014, the Company started to receive repayment of this note. This loan was fully repaid in April 2015. The Company recorded $49 and $158 for the years ended December 31, 2015 and 2014, respectively, in interest and other income (expense), net, representing cash collected during those periods.

13. Selected Quarterly Financial Data (Unaudited)

	Three Months Ended							
	Dec. 31, 2015	Sept. 30, 2015	June 30, 2015	March 31, 2015	Dec. 31, 2014	Sept. 30, 2014	June 30, 2014	March 31, 2014
Statements of Operations Data:								
Revenue	$ —	$ —	$ —	$ —	$ —	$ —	$ —	$ —
Loss from operations	(11,072)	(11,907)	(8,982)	(13,300)	(6,261)	(6,424)	(5,885)	(4,892)
Net loss	(11,017)	(11,853)	(8,957)	(13,260)	(6,208)	(6,390)	(5,851)	(4,847)
Basic and diluted net loss per share	$ (0.49)	$ (0.53)	$ (0.40)	$ (0.59)	$ (0.28)	$ (2.71)	$(11.68)	$ (9.79)

ITEM 9. *CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE*

None.

ITEM 9A. *CONTROLS AND PROCEDURES*

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2015. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2015, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Internal Control Over Financial Reporting

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) under the Exchange Act. Our internal control system is designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Our management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2015. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its 2013 *Internal Control—Integrated Framework.* Based on this assessment, our management has concluded that as of December 31, 2015, our internal control over financial reporting is effective.

As an emerging growth company, as defined under the terms of the Jobs Act of 2012, the Company's independent registered accounting firm is not required to issue an attestation report on the internal control over financial reporting.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. *OTHER INFORMATION*

Pursuant to Section 219 of the Iran Threat Reduction and Syria Human Rights Act of 2012, which added Section 13(r) of the Exchange Act, the Company hereby incorporates by reference herein Exhibit 99.1 of this report, which includes disclosures publicly filed by Novartis AG, of which Novartis BioVentures Ltd., which we consider to be our affiliate due to its stock ownership of our company, is an indirect wholly-owned subsidiary.

PART III

ITEM 10. *DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE*

The information required by this Item 10 will be included under the captions "Executive Officers," "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement to be filed with the SEC with respect to our 2016 Annual Meeting of Stockholders and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, including our principal executive, financial and accounting officers, and our directors and employees. We have posted the text of our Code of Business Conduct and Ethics under the "Investors & Media — Corporate Governance" section of our website, *www.tokaipharmaceuticals.com*. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

ITEM 11. *EXECUTIVE COMPENSATION*

The information required by this Item 11 will be included under the captions "Executive and Director Compensation" and "Compensation Committee Interlocks and Insider Participation" in our definitive proxy statement to be filed with the SEC with respect to our 2016 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 12. *SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS*

The information required by this Item 12 will be included under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans" in our definitive proxy statement to be filed with the SEC with respect to our 2016 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 13. *CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE*

The information required by this Item 13 will be included, as applicable, under the captions "Employment Agreements," "Potential Payments Upon Termination or Change in Control," "Board Determination of Independence" and "Related Person Transactions" in our definitive proxy statement to be filed with the SEC with respect to our 2016 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 14. *PRINCIPAL ACCOUNTANT FEES AND SERVICES*

The information required by this Item 14 will be included under the captions "Audit Fees and Services" and "Pre-Approval Policies and Procedures" in our definitive proxy statement to be filed with the SEC with respect to our 2016 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

ITEM 15. *EXHIBITS AND FINANCIAL STATEMENT SCHEDULES*

(a) *Financial Statements*

For a list of the consolidated financial statements included herein, see Index to the Consolidated Financial Statements on page 93 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(b) *Exhibits*

The exhibits filed as part of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding such Exhibits, which Exhibit Index is incorporated herein by reference.

(c) *Financial Statement Schedules*

No financial statement schedules have been submitted because they are not required or are not applicable or because the information required is included in the consolidated financial statements or the notes thereto.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

TOKAI PHARMACEUTICALS, INC.

Date: March 10, 2016

By: /s/ Jodie P. Morrison
Jodie P. Morrison
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Jodie P. Morrison Jodie P. Morrison	President, Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2016
/s/ Lee H. Kalowski Lee H. Kalowski	Chief Financial Officer (Principal Financial and Accounting Officer)	March 10, 2016
/s/ Seth L. Harrison Seth L. Harrison	Chairman of the Board	March 10, 2016
/s/ Timothy J. Barberich Timothy J. Barberich	Director	March 10, 2016
/s/ Stephen Buckley, Jr. Stephen Buckley, Jr.	Director	March 10, 2016
/s/ Cheryl L. Cohen Cheryl L. Cohen	Director	March 10, 2016
/s/ David A. Kessler David A. Kessler	Director	March 10, 2016
/s/ Joseph A. Yanchik III Joseph A. Yanchik III	Director	March 10, 2016

EXHIBIT INDEX

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's current report on Form 8-K (File No. 001-36620) filed on September 26, 2014)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's current report on Form 8-K (File No. 001-36620) filed on September 26, 2014)
4.1	Specimen certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.1	Fifth Amended and Restated Investor Rights Agreement, dated as of May 13, 2013, among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.1 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.2+	2007 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.3+	Form of Incentive Stock Option Agreement under 2007 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.4+	Form of Nonstatutory Stock Option Agreement under 2007 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.5+	2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.6+	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.7+	Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.8+	2014 Employee Stock Purchase Plan to (incorporated by reference to Exhibit 10.17 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.9+	Amended and Restated Employment Agreement, dated as of July 16, 2014, between the Registrant and Jodie P. Morrison (incorporated by reference to Exhibit 10.8 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.10+	Amendment to Employment Letter, dated as of January 15, 2015, between the Registrant and Jodie P. Morrison (incorporated by reference to Exhibit 10.10 to the Registrant's Annual Report on Form 10-K (File No. 001-36620) filed on March 26, 2015)
10.11+	Employment Agreement, dated as of January 30, 2014, between the Registrant and John S. McBride (incorporated by reference to Exhibit 10.15 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.12+	Amendment to Employment Letter, dated as of January 15, 2015, between the Registrant and John S. McBride (incorporated by reference to Exhibit 10.12 to the Registrant's Annual Report on Form 10-K (File No. 001-36620) filed on March 26, 2015)

10.13+	Employment Agreement, dated as of April 7, 2014, between the Registrant and Karen J. Ferrante, M.D. (incorporated by reference to Exhibit 10.6 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.14+	Amendment to Employment Letter, dated as of January 15, 2015, between the Registrant and Karen J. Ferrante (incorporated by reference to Exhibit 10.14 to the Registrant's Annual Report on Form 10-K (File No. 001-36620) filed on March 26, 2015)
10.15+	Employment Agreement, dated as of August 21, 2014, between the Registrant and Lee H. Kalowski (incorporated by reference to Exhibit 10.18 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.16+	Amendment to Employment Letter, dated as of January 15, 2015, between the Registrant and Lee H. Kalowski (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-36620) filed on March 26, 2015)
10.17+†	Employment Letter, dated as of April 7, 2015, between the Registrant and Gerald E. Quirk. (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36620) filed on August 12, 2015)
10.18+	Form of Director and Officer Indemnification Agreement (incorporated by reference to Exhibit 10.13 to the Registrant's registration statement on Form S-1/A (File No. 333-198052) filed on September 2, 2014)
10.19	Sublease Agreement, dated as of February 27, 2015, between the Registrant and Boston Private Wealth LLC (incorporated by reference to Exhibit 10.18 to the Registrant's Annual Report on Form 10-K (File No. 001-36620) filed on March 26, 2015)
10.20	Lease, executed on June 9, 2015, between the Registrant and 255 State Street LLC. (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36620) filed on August 12, 2015)
10.21†	Master License Agreement, dated as of May 19, 2006, between the Registrant and the University of Maryland, Baltimore, as amended by First Amendment, dated as of March 3, 2009, Second Amendment, dated as of April 10, 2012, and Third Amendment, dated as of October 28, 2013 (incorporated by reference to Exhibit 10.14 to the Registrant's registration statement on Form S-1 (File No. 333-198052) filed on August 11, 2014)
10.22†	License Agreement, dated as of January 9, 2015, between the Registrant and The Johns Hopkins University (incorporated by reference to Exhibit 10.20 to the Registrant's Annual Report on Form 10-K (File No. 001-36620) filed on March 26, 2015)
10.23†	Master Collaboration Agreement, dated January 12, 2015, between the Registrant and Qiagen Manchester Limited (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36620) filed on May 12, 2015)
12.1*	Calculation of Consolidated Ratios of Earnings to Fixed Charges and Consolidated Ratios of Earnings to Combined Fixed Charges and Preferred Stock Dividends
23.1*	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
31.1*	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1#	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2#	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

99.1*	Section 13(r) Disclosure
101INS	XBRL Instance Document.
101SCH	XBRL Taxonomy Extension Schema Document.
101CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101LAB	XBRL Taxonomy Extension Labels Linkbase Document.
101PRE	XBRL Taxonomy Extension Presentation Linkbase Document.
101DEF	XBRL Taxonomy Extension Definition Linkbase Document.

* Filed herewith.
† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.
+ Indicates management contract or plan.
# This certification will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

Exhibit 12.1

CALCULATION OF CONSOLIDATED RATIOS OF EARNINGS TO FIXED CHARGES AND CONSOLIDATED RATIOS OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS

(dollars in thousands)

	For Years Ended December 31,			
	2015	2014	2013	2012
Earnings (loss):				
Net Loss	$(45,087)	$(23,296)	$(15,819)	$(9,683)
add: Fixed charges (see below)	278	173	122	114
	$(44,809)	$(23,123)	$(15,697)	$(9,569)
Fixed charges:				
Interest expense on portion of rent expense representative of interest	$ 278	$ 173	$ 122	$ 114
Total fixed charges	$ 278	$ 173	$ 122	$ 114
Consolidated ratios of earnings to fixed charges (1)	N/A	N/A	N/A	N/A
Deficiency of earnings available to cover fixed charges	$(45,087)	$(23,296)	$(15,819)	$(9,683)
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ —	$ (94)	$ (34)
Consolidated ratios of earnings to combined fixed charges and preferred stock dividends (2)	N/A	N/A	N/A	N/A
Deficiency of earnings available to cover combined fixed charges and preferred stock dividends	$(45,087)	$(23,296)	$(15,913)	$(9,717)

(1) We did not record earnings for the years ended December 31, 2015, 2014, 2013 and 2012. Accordingly, our earnings were insufficient to cover fixed charges for such periods, and we are unable to disclose a ratio of earnings to fixed charges for such periods.

(2) We did not record earnings for the years ended December 31, 2015, 2014, 2013 and 2012. Accordingly, our earnings were insufficient to cover fixed charges and preferred stock dividends for such periods, and we are unable to disclose a ratio of earnings to combined fixed charges and preferred stock dividends for such periods.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Forms S-3 (No. 333-207359) and S-8 (Nos. 333-203032, and 333-200413) of Tokai Pharmaceuticals, Inc. of our report dated March 10, 2016 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 10, 2016

Exhibit 31.1

CERTIFICATIONS

I, Jodie P. Morrison, certify that:

1. I have reviewed this Annual Report on Form 10-K of Tokai Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2016

By: /s/ Jodie P. Morrison
Jodie P. Morrison
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Lee H. Kalowski, certify that:

1. I have reviewed this Annual Report on Form 10-K of Tokai Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2016

By: /s/ Lee H. Kalowski
Lee H. Kalowski
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Tokai Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jodie P. Morrison, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 10, 2016

By: /s/ Jodie P. Morrison
Jodie P. Morrison
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Tokai Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Lee H. Kalowski, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 10, 2016

By: /s/ Lee H. Kalowski
Lee H. Kalowski
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 99.1

Section 13(r) Disclosure

The disclosures reproduced below with respect to the fiscal year ended December 31, 2015 were publicly filed with the Securities and Exchange Commission by Novartis AG on its Form 20-F (File No. 001-15024) on January 27, 2016, and are filed as an exhibit to this Annual Report on Form 10-K in accordance with Section 13(r) of the Securities Exchange Act of 1934, as amended. Novartis BioVentures, Ltd., which we consider to be our affiliate due to its stock ownership of our company, is an indirect wholly-owned subsidiary of Novartis AG. We have not independently verified or participated in the preparation of this disclosure.

From Novartis AG's Form 10-K for year ended December 31, 2015

Disclosure pursuant to Section 219 of the Iran Threat Reduction & Syria Human Rights Act (ITRA)

At Novartis, it is our mission to discover, develop and successfully market innovative products to prevent and cure diseases, to ease suffering and to enhance the quality of life of all people, regardless of where they live. This mission includes the compliant sale of medicines and other healthcare products worldwide. To help us fulfill this mission, we have representative offices located in Iran.

As of October 18, 2010, a non-US affiliate within our Pharmaceuticals Division entered into a non-binding Memorandum of Understanding (MoU) with the Ministry of Health and Medical Education of the Islamic Republic of Iran. Pursuant to the MoU, the Iranian Ministry of Health acknowledges certain benefits that may apply to sales of certain Novartis Pharmaceuticals medicines by third-party distributors in Iran. These include fast-track registration, market exclusivity, end-user subsidies and exemptions from customs tariffs. Novartis receives no payments from the Iranian Ministry of Health under the MoU and the MoU creates no obligations on the part of either Novartis or the Iranian Ministry of Health.

In 2015, non-US affiliates relating to our Pharmaceuticals and Sandoz Divisions made payments to government entities in Iran related to exit fees and other transactions ordinarily incident to travel by doctors and other medical professionals resident in Iran to attend conferences or other events outside Iran.

From time to time, including in 2015, non-US affiliates relating to our Pharmaceuticals and Sandoz Divisions enter into agreements with hospitals, research institutes, medical associations and universities in Iran to provide grants, sponsor congresses, seminars and symposia, and with doctors and other healthcare professionals for consulting services, including participation in advisory boards and investigator services for observational (non-interventional) studies. Some of these hospitals and research institutes are owned or controlled by the government of Iran, and some of these doctors and healthcare professionals are employed by hospitals that may be public or government-owned.

Because our Pharmaceuticals and Sandoz Divisions have operations in Iran, including employees, they obtain services and have other dealings incidental to their activities in that country, including paying taxes and salaries, and obtaining office rentals, insurance, electricity, water and telecommunications services, office and similar supplies and customs-related services from Iranian companies that may be owned or controlled by the government of Iran.

Some beneficiaries of payments made by non-US affiliates relating to our Pharmaceuticals and Sandoz Divisions in the course of the operations described above maintain accounts at banks that are included on the list of Specially Designated Nationals (SDNs). Nonetheless, since such payments relate to lawful and authorized transactions, use of a blocked Iranian financial institution is permitted in accordance with applicable laws and given that such institution is identified on the SDN List with the tag [IRAN].