May 12, 2015

HEALTHCARE/BIOTECHNOLOGY

Stock Rating:

OUTPERFORM

12-18 mo. Price Target	$38.00
TKAI - NASDAQ	$10.05

3-5 Yr. EPS Gr. Rate	NA
52-Wk Range	$30.00-$9.67
Shares Outstanding	22.4M
Float	6.6M
Market Capitalization	$225.2M
Avg. Daily Trading Volume	58,188
Dividend/Div Yield	NA/NM
Book Value	NA
Fiscal Year Ends	Dec
2015E ROE	NA
LT Debt	NA
Preferred	NA
Common Equity	NA
Convertible Available	No

Trading range is as of 9/23/14 IPO.

EPS Diluted	Q1	Q2	Q3	Q4	Year	Mult.
2014A	NA	NA	(2.70)	(0.28)	(3.60)	NM
2015E	(0.30)	(0.34)	(0.47)	(0.51)	(1.62)	NM
2016E	--	--	--	--	(2.15)	NM

Tokai Pharmaceuticals, Inc.

A Novel Agent Treating Prostate Cancer Where Others Fail; Initiate w/Outperform

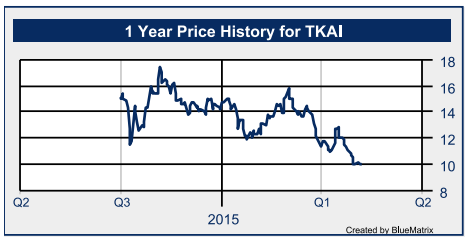
SUMMARY

We are initiating coverage of Tokai Pharmaceuticals, Inc. (TKAI) with an Outperform rating and a 12- to 18-month price target of $38. TKAI's flagship compound galeterone initially addresses a clear unmet medical need in prostate cancer, i.e. castration-resistant prostate cancer (CRPC) patients with tumor-expressing androgen receptor (AR) split variants (AR-V7) for whom recently approved novel agents such as Zytiga and Xtandi are not expected to be effective. We view TKAI shares as having significant upside potential (phase III start 1H15, pivotal data 2H16), given a clear/favorable regulatory pathway, a high probability of phase III success, sizeable market opportunity (addressing a key resistance mechanism to novel therapies) and no foreseeable competition.

KEY POINTS

- **Galeterone targets a clear unmet need.** Emerging data strongly suggest AR spliced variants (C-terminal loss or loss of the ligand binding domain/LBD) may render primary resistance to novel AR-targeting therapies such as Zytiga and Xtandi. Galeterone showed efficacy in the C-terminal loss/AR-V7 patients where Zytiga and Xtandi are not effective.
- **Phase III trial has high probability of success.** The ARMOR3 trial, the first biomarker guided pivotal trial in CRPC, will compare rPFS vs. Xtandi in AR-V7+ patients. We project a 75% probability of success based on clear MOA, promising efficacy seen in ARMOR2 trial, and Xtandi's lack of efficacy in AR-V7+ mCRPC patients.
- **Novel multi-mechanisms of action offer key advantages.** As compared to Zytiga, galeterone does not require concurrent use of steroid, thereby sparing steroid-associated AEs. As compared to Xtandi, galeterone should not have the risk of causing seizures since it is not a GABA receptor antagonist.
- **Galeterone addresses a large market.** AR-V7+ prevalence tends to increase following subsequent treatment lines (25%, 51% and 67% in post-Zytiga, post-Xtandi and post both treatments, respectively). We believe galeterone has significant potential in the resistant subset and project US peak sales of ~$1.4B by 2025.

Stock Price Performance



Company Description

Tokai Pharmaceuticals, Inc., a clinical-stage biopharmaceutical company, focuses on developing novel proprietary therapies for the treatment of prostate cancer and other hormonally-driven diseases in the US.

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Investment Thesis

We are initiating coverage of Tokai Pharmaceuticals, Inc. (TKAI) with an Outperform rating and a 12- to 18-month price target of $38. Castration resistant prostate cancer (CRPC) with tumor-expressing androgen receptor (AR) split variants (in particular AR-V7) appear to be associated with primary resistant to Zytiga and Xtandi potentially due to the loss of ligand-binding domain (LBD) which is required for these drugs to function. TKAI's flagship compound galeterone is a highly selective, multi-targeted small molecule that disrupts the AR signaling. We believe that galeterone addresses a clear unmet medical need in prostate cancer, in which recently approved novel agents such as Zytiga and Xtandi are not expected to be effective. Currently, a bio-marker guided pivotal phase III trial is being prepared in AR-V7+ metastatic CRPC patients (M1 patients) with a planned initiation in 1H15. We view TKAI shares as having significant upside potential (pivotal phase III data 2H16), given a clear/favorable regulatory pathway, a high probability of phase III success, sizeable market opportunity (addressing a key resistance mechanism to novel therapies) and no foreseeable competition.

Galeterone targets a clear unmet need

Although several novel drugs targeting the AR signaling such as Xtandi by Medivation and Zytiga by Johnson & Johnson have brought major breakthroughs to the treatment of metastatic CRPC (mCRPC), approximately 20-40% of patients do not have PSA response to these agents, i.e. have primary resistance. Additionally, among patients who initially have a response to Xtandi or Zytiga, virtually all patients eventually acquire secondary resistance. One of the possible mechanisms driving the resistance to both agents may involve the presence of androgen receptor splice variants. These alternatively spliced variants encode a truncated AR protein that lacks the C-terminal ligand-binding domain (LBD) but retains the trans-activating N-terminal domain. Although the resultant truncated proteins are unable to bind ligand, they are constitutively active as transcription factors and capable of promoting activation of target genes. AR-V7 is the most abundant AR splice variant that causes C-terminal loss in AR. The prevalence of AR-V7 also increases significantly post treatment with Xtandi or Zytiga. Emerging clinical data from several groups (Johns Hopkins, MD Anderson and Memorial Sloan-Kettering Cancer Center) strongly suggest that AR splice variants appear to be associated with resistance to Xtandi and Zytiga.

Galeterone's initial clinical focus is in mCRPC patients whose tumors express AR-V7. In phase II ARMOR2 trial, galeterone induced a PSA response in six out of seven AR-V7 positive patients. As a comparison, clinical trials conducted by various groups showed both Zytiga and Xtandi have limited activity in AR-V7-positive population including low PSA response, short PSA or radiographic progression-free survival (PFS) and short overall survival.

We believe the phase III ARMOR3 trial has a high probability of success

The phase III ARMOR3 trial (1H15 start) will compare the safety and efficacy of galeterone vs. Xtandi in M1 CRPC patients with detectable AR-V7 in circulating tumor cells (CTC) who have not received second generation anti-androgens (e.g. Zytiga, Xtandi) and chemotherapy. TKAI has finalized the trial design with the FDA, Canada and the EU regulatory agency. We see the trial design (frontline M1 CRPC vs. Xtandi and primary endpoint of radiographic progression free survival (PFS) in a small number of patients, n=148) as highly favorable since it requires only a small number of patients, short follow-up time and spares potential negative impact from follow-on therapies (vs. if OS were the primary endpoint).

We believe the phase III trial has a high probability of success (we project a 75% probability of success) based on the strong mechanism of action, pre-clinical data as well as the promising retrospective analysis of the phase II ARMOR2 trial in AR-V7 positive patients. The phase III trial was powered at 90% to detect an 82% increase in median rPFS in galeterone arm vs. the Xtandi arm. The phase II ARMOR2 trial showed a median time to PSA progression (TTPP) of 7.3 months, which represents a 247% improvement over the median rPFS of Xtandi-treated patients in historical control in the Johns Hopkins study. Although we caution investors the limitation of comparing results cross different trials, since the patient polution in the two studies differs (treatment naive in ARMOR2 trial vs. previously treated patients in Xtandi-treated patients in the Johns Hopkins trial), we still see the phase III trial has sufficient room for success, especially given that time to PSA progression should come earlier than rPFS (i.e., rPFS should be longer than TTPP) in mCRPC patients.

Currently the companion diagnostic test to detect AR-V7 in CTC is at the final stage to being validated and finalized at Johns Hopkins. The phase III trial appears on track to start screening and dosing patients in 1H15 once the diagnostic test is finalized.

Novel multi-mechanisms of action offer galeterone key advantages over both Zytiga and Xtandi

Unlike galeterone, neither Xtandi nor Zytiga have the mechanism of AR degradation; therefore, they tend to be inactive in tumors where the ligand binding domain (LBD) is lost. Galeterone can still degrade AR even in tumors in which the LBD of AR is lost. In addition to the potential efficacy in the C-terminal loss patients, galeterone also potentially offers AE advantage and convenience of use. As compared to Zytiga, galeterone does not require concurrent use of steroid because it has more optimal activity against the lyase of CY17 relative to the hydroxylase of CY17. Therefore, galeterone could spare the side effects associated with long-term steroid use. Additionally, galeterone is not a GABA antagonist, and therefore, should not cause seizure, which is a dose-related adverse effect (AE) associated with Xtandi treatment.

Galeterone addresses a large market

AR-V7+ is present in ~12% - mid 20% of the M1 CRPC patients before treatment of Xtandi and Zytiga (according to various sources), but the prevalence tends to increase significantly following subsequent treatment lines (25%, 51% and 67% in post Zytiga, post Xtandi and post both treatments, respectively). We believe galeterone has significant potential in the resistant subset since existing therapies are not effective. Additionally, we see very little competitive risk since no other drug is currently in clinical development targeting the same patient population (to the best of our knowledge). Although galeterone's initial indication is in the frontline M1 CRPC patients with tumor-expressing AR-V7, we believe that off-label use in AR-V7 positive patient's post-Xtandi and Zytiga treatment is highly likely given the lack of effective therapy. We project galeterone US peak sales of ~$1.4B in 2025, which includes sales in the frontline M1 CRPC patients of ~$800M and sales in AR-V7 positive patients post-Xtandi and Zytiga treatment of $570M.

Company Description

Tokai Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focusing on developing novel proprietary therapies for the treatment of prostate cancer and other hormonally-driven diseases. Its lead drug candidate galeterone is a highly selective, multi-targeted, oral small molecule drug candidate for the treatment of prostate cancer via disrupting androgen receptor (AR) signaling. Galeterone is currently in a pivotal phase III trials preparations (with a potential 1H15 start) for the treatment of frontline M1 CRPC patients who express AR-V7. The company was founded in 2004 and is based in Cambridge, Massachusetts.

Valuation

We value the shares of TKAI based on risk-adjusted NPV of galeterone of ~$923M (~$38/share). We project galeterone US sales of $1.2B in 2023 and ex-US sales of ~$748M in 2023. We assume the company will out-license the ex-US right to potential partner (royalty rate of ~20%). We use a biotech typical revenue multiple of 5x and royalty multiple of 10, a probability of success of 75%, discount rate of 30% (which reflects the development stage of the company) to derive the risk-adjusted NPV of galeterone.

Risks

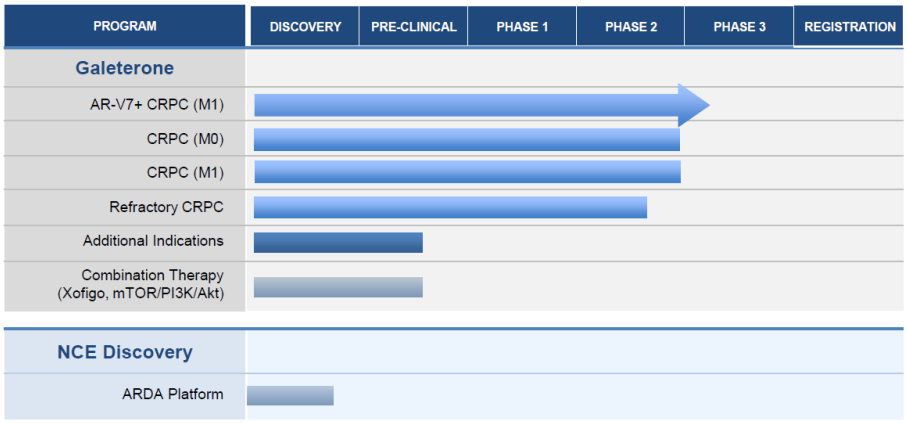
- **Clinical risks.** We view clinical risks associated with galeterone as the main risk for TKAI. Galeterone is TKAI's main asset. Galeterone may not succeed in the phase III trial. Any setbacks and/or delays in the clinical development of galeterone may generate downward pressure on the stock.
- **Regulatory risks**: Galeterone may not obtain regulatory approval in the US despite successful clinical development. A potential delay in regulatory decision may cause near-term weakness as well.
- **Commercialization risks:** The market potential and penetration of Galeterone may not be as large as our projections.
- **Financing risk.** We don't expect the company to reach profitability in the foreseeable future. Potential equity financing may result in share dilution.
- **High stock price volatility**: High stock price volatility is common among developmental companies in the biotechnology sector.

Upcoming Catalysts

- Potential to initiate the phase III ARMOR3 trial in frontline M1 CRPC patients with detectable AR-V7 in CTC (1H15)
- Potential to report top line data from the pivotal phase III ARMOR3 trial of galeterone in patients with AR-V7+ tumors (2H16)
- Potential business development activities for galeterone (TBD)

Pipeline Programs

Exhibit 1. TKAI Programs

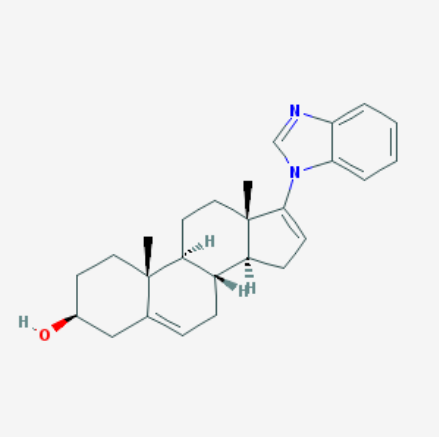


Source: Company reports

Galeterone Background

Galeterone is an oral small molecule that disrupts the androgen receptor signaling pathway via three mechanisms of action. The AR signaling pathway is the primary pathway that drives prostate cancer growth. The development of galeterone is initially focused on a unique unmet medical need, i.e. in the subset of castration resistant prostate cancer (CRPC) patients, in which prostate tumor cells express an altered androgen receptor that lacks the ligand binding domain (LBD, also called "C-terminal loss"), for which currently available AR targeting therapies including Xtandi and Zytiga are not expected to be effective. One of galeterone's mechanisms of action, androgen receptor degradation, enables it to be effective in patients where the truncated androgen receptors are missing the LBD.

Exhibit 2. Galeterone Structure



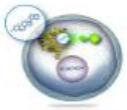
Source: Medical Literature

Three mechanisms of actions to target androgen receptor pathway

Androgen receptor (AR) signaling is a critical pathway that drives the growth of prostate cancer cells. The pathway is often activated by the binding of androgens, such as testosterone and DHT, to the ligand binding domain (LBD) of androgen receptors (AR) in prostate cancer cells. Androgen-deprivation therapy (ADT) remains the principal treatment for patients with locally advanced and metastatic disease. Persistent androgen receptor signaling despite low levels of serum androgens has been identified as a critical target for drug discovery in CRPC. The overall survival benefit and the approval of two androgen receptor-targeted agents, Zytiga and Xtandi, serve as the proof of principle that the androgen receptor remains relevant in CRPC.

Galeterone disrupts the AR signaling pathway via three mechanisms of action. First, it inhibits the enzyme CYP17 and blocks the synthesis of testosterone. Second, it is an androgen receptor antagonist and blocks the binding of testosterone or DHT with the androgen receptor. Third, it degrades androgen receptor and reduces the amount of androgen receptor protein in tumor cells. As a comparison, neither Zytiga nor Xtandi, the two approved therapies for metastatic CRPC, can degrade AR. Rather, both compounds require the presence of the LBD domain of the AR to function, rendering their lack of efficacy in mutant AR which lacks the LBD.

Exhibit 3. Galeterone Has Three Mechanisms of Action Targeting AR Signaling

	CYP17 Lyase Inhibitor	*AR Antagonist*	*AR Degrader*
	 *Inhibits androgen synthesis*	 *Blocks androgen binding*	 *Decreases AR levels*
Abiraterone	✓		
Enzalutamide		✓	
Galeterone	✓ • No mandatory steroids • Fasting not required • IC_{50} = 0.023 to 0.047μM[5,6]	✓ • Not a $GABA_A$ antagonist • No seizures • IC_{50} = 0.6μM[7]	✓ • Active in C-terminal loss/ AR-V7 splice variants • IC_{50} = 1μM[8]

Source: Company reports

- **CYP17 lyase inhibition**

Galeterone inhibits CYP17, which plays a central role in synthesizing the androgens that drive tumor cell growth. CYP17 has two enzymatic activities: lyase and hydroxylase. Blocking the lyase activity of CYP17 can decrease the production of key androgen precursors, while blocking the hydroxylase activity causes an accumulation of certain steroids, such as progesterone, deoxycorticosterone and corticosterone, and a reduction in cortisol, which can result in mineralocorticoid excess and require co-administration of steroids. In preclinical studies, galeterone was shown to 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. Clinical trial showed consistent results that galeterone has not caused mineralocorticoid excess and, as a result, does not require co-administration of steroids.

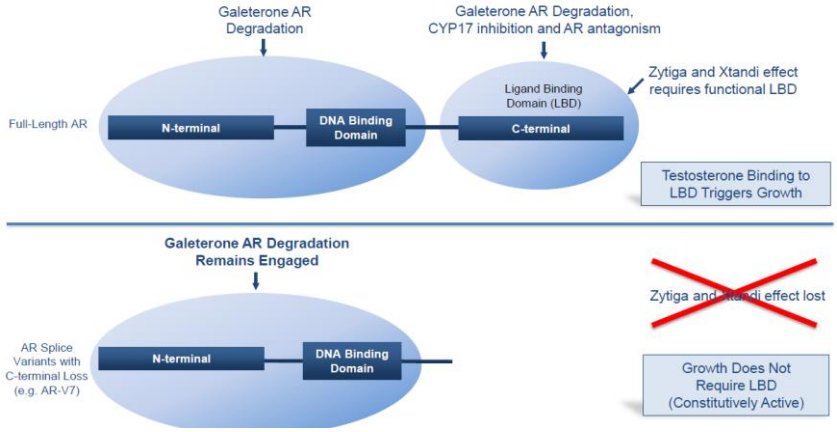
- **Androgen receptor antagonist**

Galeterone blocks androgens from binding to the AR, which results in reduced translocation of the AR into the cell nucleus, prevents the AR from acting as a transcription factor and decreases the expression of androgen-responsive genes that drive tumor growth. Compared to conventional anti-androgens such as bicalutamide, Xtandi binds to the receptor with higher affinity, prevents nuclear translocation and DNA binding, and induces apoptosis without agonist activity in preclinical models. However, a potentially concerning adverse effect of Xtandi is the occurrence of seizures. The mechanism of seizures is thought to be related to inhibition of gamma-aminobutyric acid (GABA) receptors in the brain. Galeterone is not a GABA antagonist; therefore theoretically it does not have the risk of causing seizures, as compared to Xtandi.

- **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. Galeterone was shown to degrade AR in varying degrees in prostate cancer cell lines that express both non-mutated full-length AR and multiple forms of AR alterations, including splice variants, such as AR-V7, that are missing large portions of the protein sequence of the AR in the C-terminus.

Exhibit 4. AR Degradation Provides Galeterone Unique Opportunity for AR-V7+/C-terminal Loss



Source: Company Documents

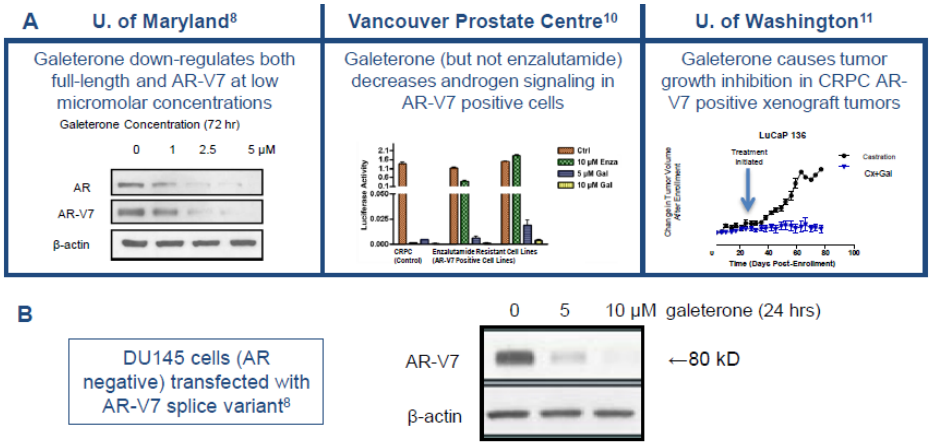
Galeterone should have advantages over both Zytiga and Xtandi

- **Efficacy in tumors that are resistant to Zytiga or Xtandi**

Unlike galeterone, neither Xtandi nor Zytiga has the mechanism of AR degradation; therefore, they tend to be inactive in tumors where the ligand binding domain (LBD) is lost since they both require the LBD to function. Galeterone, however, can still degrade AR, even in tumors in which the LBD of AR is lost.

Preclinical studies conducted by different groups showed that galeterone was able to down-regulate the production of both full length AR and AR-V7, the AR signaling, and inhibit the tumor growth in xenograft model transfected with CRPC AR-V7 mutant (Exhibit 5). As a comparison, Xtandi was shown to be inactive in down-regulating the AR signaling in AR-V7 positive cells.

Exhibit 5. Galeterone Down-regulates the Production of AR-V7 and AR Signaling



Sources: Company Reports

- **Potentially better AE profile over Zytiga and Xtandi**

As compared to Zytiga, galeterone does not require concurrent use of steroid because it has more optimal activity against the lyase of CY17 relative to the hydroxylase of CY17. Therefore, galeterone could potentially spare the side effects associated with long-term steroid use and is more convenient to use as compared to Zytiga. Galeterone is not a GABA antagonist; therefore, it should not cause seizure, which is a dose-related AE associated with Xtandi treatment.

Unmet Medical Need in CRPC

It is widely accepted that CRPC continues to rely on androgen signaling. Several novel drugs have recently emerged for the treatment of CRPC, either by suppressing the synthesis of androgens or targeting the androgen receptor (AR) directly. Xtandi is an inhibitor of androgen-receptor signaling that exerts its activity by binding avidly to the ligand-binding domain/LBD of the AR, competing with and displacing the natural ligands of this receptor (testosterone and dihydrotestosterone) while also inhibiting translocation of the AR into the nucleus and impairing transcriptional activation of androgen-responsive target genes. Zytiga is an inhibitor of cytochrome P450 17A1 (CYP17A1) that impairs androgen-receptor signaling by depleting adrenal and intratumoral androgens. Both drugs have showed improvement in survival and were approved by the FDA for the treatment of metastatic CRPC.

Although Xtandi and Zytiga brought major breakthroughs to the treatment of metastatic CRPC, approximately 20-40% of patients do not have PSA response to these agents, i.e. primary resistance. Additionally, among patients who initially have a response to Xtandi or Zytiga, virtually all patients eventually acquire secondary resistance.

AR Alternative Splice Variants

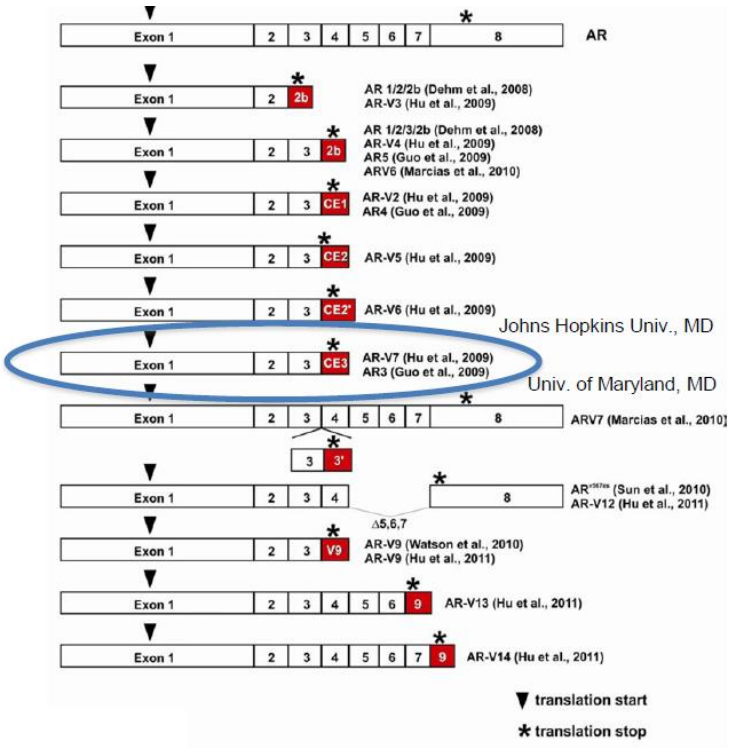
One of the possible mechanisms for the resistance to both agents may involve the presence of androgen receptor splice variants. These alternatively spliced variants encode a truncated AR protein that lacks the C-terminal ligand-binding domain (LBD) but retains the trans-activating N-terminal domain. Although the resultant truncated proteins are unable to bind ligand, they are constitutively active as transcription factors and capable of promoting activation of target genes.

Because Xtandi needs the interaction with the LBD of the AR to exert its antitumor activity, it would be expected that the presence of the protein encoded by the androgen-receptor splice variant (which lacks the LBD) may be associated with drug resistance. Furthermore, since the protein encoded by the AR splice variant is ligand-independent and yet constitutively active, its activity would not be expected to be inhibited by ligand-depleting agents such as Zytiga. These hypotheses are supported by preclinical studies conducted by various groups, including the Johns Hopkins study, the MD Anderson study and the MSKCC study.

AR with C-terminal loss is constitutively active

Androgen receptor is made of 8 exons. Exon 1 encodes N-terminal domain containing transcriptional activation sites. Exons 2-4 encode DNA-binding domain and exons 5-8 encode ligand-binding domain (LBD). Alternative spliced variants (lacking LBD) are constitutively active. They can bind to DNA and activate transcription independent of ligands.

Exhibit 6. Androgen Receptor and Alternative Splice Variants



Sources: Company reports

AR-V7 is the most important AR variant

AR-V7 is the most abundant form of AR splice variants. It lacks a functional LBD and is constitutively active, therefore, it cannot be inhibited by LBD-targeting drugs. Additionally, the prevalence of AR-V7 increases post Zytiga and Xtandi therapies. Before Zytiga or Xtandi therapies, the prevalence of AR-V7 is estimated to be 12% to mid-20% by various groups. The prevalence of AR-V7 increases significantly after Zytiga or Xtandi therapies, reaching ~25% post Xtandi treatment, ~51% post Zytiga treatment and ~67% post both Zytiga and Xtandi treatments.

The constitutively-active AR splice variants may represent a mechanism of resistance to Zytiga and Xtandi

Even with the novel treatment of Zytiga and Xtandi, there is a small portion of the CRPC patients who are “primary resistance” who need to discontinue the treatments within four months as a result of clinical or radiologic progression. mCRPC patients with AR-V7 and AR C-terminal loss appear to be the poor prognostic factor as these patients were associated with worse clinical outcomes. In fact, the presence of truncated AR has been linked to lack of response when CRPC patients were treated with Zytiga or Xtandi in several studies conducted by various groups. These data suggest that the detection of AR-V7 in circulating tumor cells from patients with CRPC may be associated with resistance to Xtandi and Zytiga.

- **The Johns Hopkins experience**

In a prospectively designed trial, the investigators at Johns Hopkins evaluated AR-V7 messenger RNA in circulating tumor cells (CTC) from patients treated with Xtandi or Zytiga and examined the association between the status of AR-V7 and PSA response, PSA progression-free survival (or PSA PFS).

A total of 31 Xtandi-treated patients and 31 Zytiga-treated patients were enrolled, of whom 39% and 19% had detectable AR-V7 in circulating tumor cells, respectively. In both arms, AR-V7-positive patients had lower PSA response rates than AR-V7-negative patients (0% vs. 53%, P = 0.004 for Xtandi-treated patients; 0% vs. 68%, P = 0.004 for Zytiga treated patients), shorter median PSA PFS (1.4 months vs. 6.0 months; P<0.001; and 1.3 months vs. not reached; P<0.001 for Xtandi and Zytiga treated patients respectively), clinical or radiographic PFS (2.1 months vs. 6.1 months; P<0.001; and 2.3 months vs. not reached; P<0.001 for Xtandi and Zytiga treated patients, respectively).

Exhibit 7. AR-V7+ Patients Respond Worse to Zytiga or Xtandi Treatment

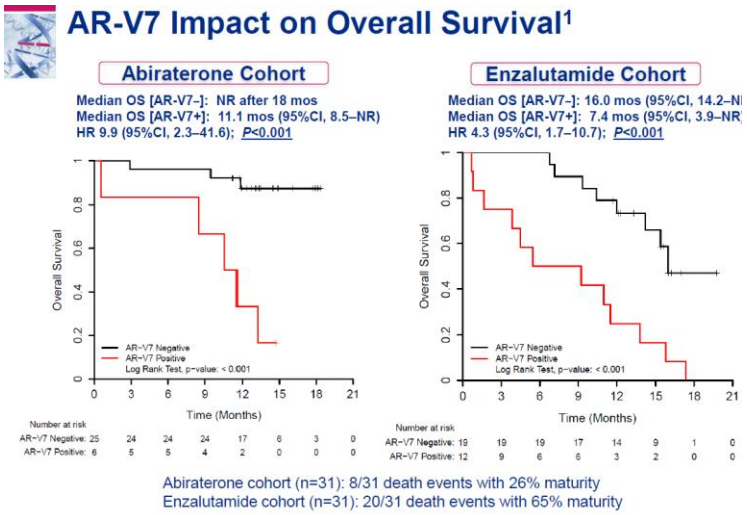
Treatment	Hopkins Expanded Data Set[1]				
	AR-V7 status	PSA50	PSA Progression-Free Survival	rPFS (mos)	OS (mos) (95% CI)
Zytiga (N=31)	+	0%*	1.3	2.3 **	11.1 (8.5–NR)**
	–	68%	>5.3	>6.3	NR (>18 mos)
Xtandi (N=31)	+	0%*	1.4	2.1**	7.4 (3.9–NR)**
	–	53%	6.0	6.1	16.0 (14.2–NR)

PSA Response → PSA Progression → Scan Progression → Death

Source: Company reports

The status of AR-V7 also appears to predict overall survival, with mOS of 5.5 months vs. not reached; P = 0.002; 10.6 months vs. not reached, P = 0.006, for Xtandi and Zytiga-treated patients, respectively (Exhibit 8).

Exhibit 8. AR-V7+ Patients Respond Worse to Zytiga or Xtandi Treatment



Sources: ESMO, 2014

- **The MD Anderson experience**

The group at MD Anderson conducted a prospectively designed phase II trial in which 60 patients with bone mCRPC received a sequential combination regimen of Zytiga and Xtandi. Data from the trial were presented during the 2014 American Society of Clinical Oncology (ASCO) conference. In the subset of 15 patients who were evaluable for C-terminal loss, four patients were identified as having C-terminal loss, including two identified as having AR-V7 (13.3%, 2/15). Antibody-based immunohistochemistry assays were used in the study to identify the presence of C-terminal loss and AR-V7. All four patients with C-terminal loss showed primary resistance (defined as discontinuation of therapy due to symptomatic or imaging evidence of disease progression within four months of initiating treatment). Of the 11 patients in the subset that did not have C-terminal loss or AR-V7, nine patients, or 82%, showed benefit (defined as discontinuation of therapy due to symptomatic or imaging evidence of disease progression at least four months after initiating treatment) (Exhibit 9).

Exhibit 9. Summary of MD Anderson C-Terminal Loss and AR-V7 Findings

	N	Primary Resistance	Benefit
AR-V7 Positive	2	100% (2/2)	0% (0/2)
C-terminal loss (e:	2	100% (2/2)	0% (0/2)
Negative for AR-V7	11	18% (2/11)	82% (9/11)

Source: 2014 ASCO & Oppenheimer & Co. Research

Investigators from MD Anderson also published the data from a second study in European Urology in May 2014. In the study, the researchers evaluated bone biopsy specimens from bone mCRPC patients that had been treated with Xtandi to evaluate the effects of Xtandi on cancer and to associate these effects with clinical observations. The group evaluated a population of 23 patients who had two evaluable biopsies for AR-V7. Based on identification of AR-V7 at baseline, 86% of the patients with AR-V7 showed primary resistance while only 38% of the patients that did not have AR-V7 showed primary resistance. The presence of AR-V7 at any time point was more common in patients with primary resistance to Xtandi (p = 0.018). Additionally, AR-V7 expression was not found in tumor specimens from patients with prolonged benefit (>6 mo).

Exhibit 10. 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)

Source: 2014 J European Urology & Oppenheimer & Co. Research

- **Memorial Sloan Kettering Cancer Center (MSKCC) experience**

Researchers from MSKCC presented data from a clinical trial at the European Society for Clinical Oncology 2014 Congress. In the trial, 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 (resistant to therapy) and 25 showed a reduction in PSA levels (clinical benefit). All patients were screened at baseline for C-terminal loss. A retrospective analysis was conducted in patients with C-terminal loss to assess whether they had primary resistance or clinical benefit. Of the six patients identified as having C-terminal loss, no patient showed a clinical benefit while 63% of the patients without C-terminal loss showed clinical benefit (Exhibit 11).

Exhibit 11. Summary of MSKCC C-Terminal Loss Findings

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

Source: 2014 ESCO

Galeterone Clinical Experience

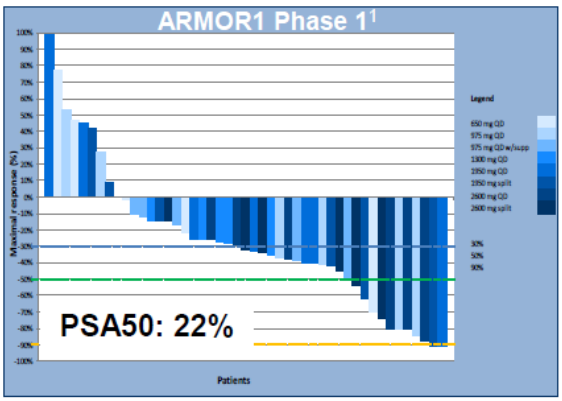
Phase I ARMOR1 trial

In November 2009, TKAI initiated a dose-escalating phase I trial, the ARMOR1 trial, evaluating galeterone in 49 CRPC patients at eight sites in the US using an earlier formulation of galeterone.

- **ARMOR1 trial design.** The ARMOR1 trial enrolled 49 CRPC patients who were either metastatic or non-metastatic CRPC treatment-naïve patients. Patients in the trial received escalating doses of galeterone ranging from 650 mg/day to 2600 mg/day either once a day or a split dose twice daily. Galeterone was taken with a patient choice of meal or with a food supplement. Patients received galeterone for the first 12 weeks followed by optional continued dosing if they can tolerate the treatment and did not show signs of disease progression. The primary endpoints for the trial included incidence of adverse events and change from baseline in safety parameters. Secondary endpoints included the rate of PSA50 or PSA nadir and changes in disease status from baseline in CT/MRI scans and bone scans over the 12-week treatment period. Of the 49 patients enrolled in ARMOR1, 37 patients completed the 12-week treatment period, and 22 patients entered the extension phase of the trial. Of the 12 patients who did not complete the 12-week treatment period, five discontinued treatment due to disease progression, five discontinued treatment due to adverse events and two voluntarily withdrew from the trial.

- **Galeterone showed PSA response.** PSA reduction was seen in each dose level tested. Of the 49 patients, 24 had a reduction of PSA by more than 30% (PSA30 of 49%) and 11 individuals had a PSA reduction of more than 50% (PSA50 of 22%). In the highest dose cohort of 2600 mg/day (n=12), 75% of the patients had PSA reduction of at least 30% and 42% of the patients had PSA reduction of at least 50%. Reductions in tumor size and overall tumor stabilization as measured by CT/MRI and bone scans were also observed in multiple patients.

Exhibit 12. Galeterone Activity in Phase I ARMOR1 Trial



Sources: Company reports

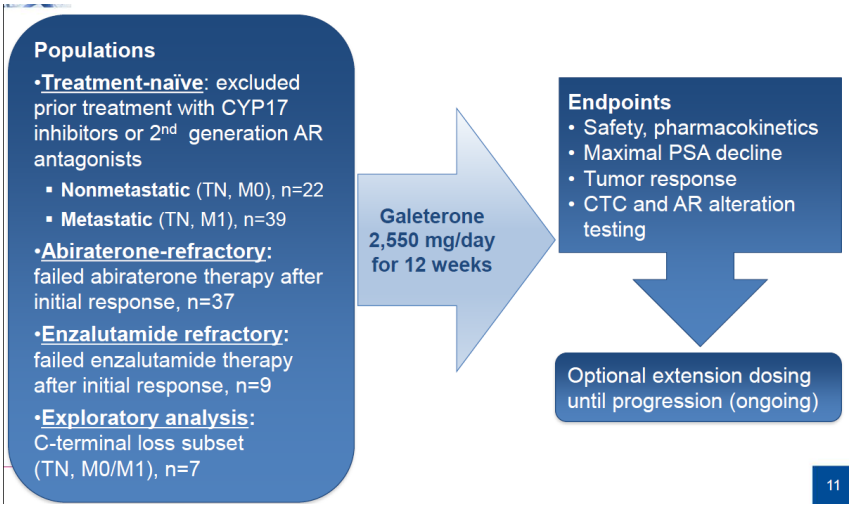
- **Galeterone was well tolerated.** Approximately 90% of treatment-emergent adverse events (TEAEs) reported for the first 12 weeks of treatment were grade 1 or grade 2 in severity. The majority were determined to be not related or unlikely related to galeterone. The most common TEAEs reported for the first 12 weeks of treatment were fatigue, increased aminotransferase, nausea, diarrhea and pruritus. The incidence of TEAEs was not dose-related. A total of eight patients (or 16%) experienced a grade 3 treatment-emergent increase in aminotransferase indicating elevated liver enzyme levels. These events were asymptomatic and transient. Of the eight patients, two patients voluntarily withdrew from the trial, and six patients restarted at the same dose level or one dose level below with no recurrence of a grade 3 or higher adverse event. A maximum tolerated dose (MTD) was not reached in the trial. There was only one unexpected sAE assessed by the investigator as possibly related to treatment with galeterone: a case involving a 77-year old patient who developed rhabdomyolysis, an acute disintegration of muscle tissue, and acute renal failure that occurred while receiving simvastatin, a statin known to be associated with rhabdomyolysis. The patient had underlying chronic renal insufficiency, renal artery stenosis and hydronephrosis requiring stents and presented after a fall, all of which are risk factors for either acute renal failure or rhabdomyolysis.

Phase II ARMOR trial supports phase III development

TKAI has modified the formulation of galeterone to eliminate the food effect. In December 2012, TKAI initiated a phase II trial, the ARMOR2 trial (**A**ndrogen **R**eceptor **M**odulation **O**ptimized for **R**esponse), evaluating galeterone in patients with treatment-resistant prostate cancer. The co-principal investigators were Bruce Montgomery, MD at the University of Washington and Mary-Ellen Taplin, MD at the Dana-Farber Cancer Institute, Harvard Medical School. The trial was funded in part by the Prostate Cancer Clinical Trials Consortium (PCCTC). Galeterone received fast-track designation from the FDA in 2012, which allows expedited review of the drug.

- **Trial design of ARMOR2.** The ARMOR2 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. The trial was conducted at 28 sites in the US and Canada. The primary endpoints of the trial included safety, PK analysis, PSA response, tumor response and AR alteration testing. Patients who responded to therapy have the opportunity to continue treatment in an extension arm of the trial.

Exhibit 13. Galeterone Phase II ARMOR2 Study Design



Sources: Company Reports

The Phase II ARMOR2 trial enrolled 112 patients, who were either treatment-naïve (n=61, including 22 patients with M0 disease and 39 patients with M1 disease), or those whose disease has progressed despite therapy with Zytiga (n=37) or Xtandi (n=9). The enrolled patients also included exploratory analysis on 7 patients with C-terminal loss (M0/M1).

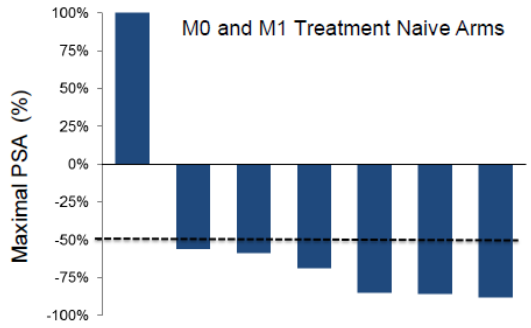
The part 1 of the trial enrolled 25 CRPC treatment-naïve patients with progressive disease and three Zytiga-refractory patients (as defined whose disease progressed during treatment with Zytiga). The CRPC treatment-naïve patients were enrolled in one of three escalating dose cohorts: 1700 mg/day, 2550 mg/day or 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. At least 50% of patients at all dose levels achieved a PSA reduction of 30% or greater. 2550 mg/day dose was chosen for the part 2 of the ARMOR2 trial. In part 2 of the trial, 108 patients were treated with 2550 mg/day dose of galeterone.

- **Galeterone showed 86% PSA50 response rate in C-Terminal loss patients**

  In a retrospective subset analysis of patients who were detected as having altered androgen receptors that were truncated in the C-terminal domain using the EPIC assay on banked CTCs, impressive PSA response was seen. Out of the seven patients with detected C-terminal loss, six showed clinically meaningful PSA reductions of at least 50%. The only patient (the seventh patient) who did not show any reduction in PSA levels discontinued therapy due to an AE unrelated to galeterone after ~six weeks in the trial and did not receive the full treatment regimen. Median time to PSA Progression (TTPP) was 7.3 months.

  We believe the clinical data in C-terminal loss patients are supportive of galeterone's mechanism of action of androgen receptor degradation, which does not require a functional ligand-binding domain.

Exhibit 14. Galeterone Induced PSA Response in C-Terminal Loss M0 and M1 Treatment Naive Patients



*Nonresponder discontinued therapy at ~6 weeks due to an unrelated adverse event

Source: 2014 EORTC & Company Reports

The interim data was presented in November 2014 during the 26th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics (EORTC-NCI-AACR conference). The interim data included patients who had not previously undergone chemotherapy and had not received treatment with Zytiga or Xtandi (or CRPC treatment-naïve patients); patients whose disease progressed during treatment with Zytiga (or Zytiga-refractory patients); and patients whose disease progressed during treatment with Xtandi (or Xtandi-refractory patients; Exhibit 15).

Exhibit 15. Galeterone Phase II ARMOR2 Patients Makeup (Interim Update)

Cohort/Subset	No.	Any PSA Decline n (%)	Best Response by RECIST 1.1 (Soft Tissue/Visceral)[b] n (%)	Best Response by PCWG2 (Bone)[b] n (%)
M0, TN	21[a]	21 (100)	No evidence of M1 at 12 weeks	No evidence of M1 at 12 weeks
M1, TN	39	35 (90)	PR 3/16 (19) SD 11/16 (69)	SD 26/36 (72)[c]
Abi-R	37	13 (35)	SD 5/15 (33)	SD 15/32 (47)
Enz-R	9	5 (56)	SD 1/3 (33)	SD 4/8 (50)
C-terminal loss, TN	7	6 (86)	SD 2/2 (100)	SD 5/5 (100)[c]

Sources: Company Reports, 2014 EORTC-AACR

Meaningful PSA response was seen in each subset, as reported below.

- In the non-metastatic and metastatic CRPC treatment-naïve patients: During the first 12 weeks of dosing, 83% of patients showed maximal reduction in PSA levels of at least 30%, and 70% of patients showed maximal reduction in PSA levels of at least 50%.

- In the metastatic CRPC treatment-naïve patients: During the first 12 weeks of dosing, 85% of patients showed maximal reduction in PSA levels of at least 30%, and 77% of patients showed maximal reduction in PSA levels of at least 50%.

- In the Zytiga-refractory patients (n=37), 13 patients showed a reduction in PSA levels. In the Xtandi-refractory patients (n=9), five showed a reduction in PSA levels.

- **Galeterone was well tolerated**

  Overall, ~90% of treatment emergent AEs (TEAEs) were grade 1 or 2 in severity. Most common TEAEs were nausea, fatigue, pruritus, decreased appetite, diarrhea, hypokalemia, and vomiting. Approximately 92% of TEAEs were grade 1 or 2 in severity in the C-terminal loss patients. No treatment related SAEs reported in the C-terminal loss patients and only 1 grade 3 related AE. In ARMOR2 trial, there were three unexpected serious adverse events (SAEs) that were assessed by the investigators as possibly related to treatment with galeterone. The SAEs included a case of angioedema in a patient who was taking a medication associated with angioedema, an episode of dizziness and fainting in a patient with a history of nausea, diabetes and hypertension who had discontinued treatment with galeterone four days prior to the episode, and a case of hypocalcemia and hyperparathyroidism in a patient with a history of hypokalcemia and hyperparathyroidism.

Exhibit 16. Galeterone ARMOR2: Adverse Events

Treatment-Emergent Related AEs in ≥10% of Patients or Any CTCAE Grade 3/4 (N=107)		
	CTCAE All Grades, n (%)	CTCAE Grade 3/4, n (%)
Nausea	38 (35.5)	1 (<1)
Fatigue	37 (34.6)	5 (4.7)
Pruritus	32 (29.9)	6 (5.6)
Decreased appetite	22 (20.6)	0
Diarrhea	18 (16.8)	1 (<1)
Hypokalemia	16(15.0)	3 (2.8)
Vomiting	15 (14.0)	0
ALT increased	13 (12.1)	7 (6.5)
AST increased	14 (13.1)	4 (3.7)
Hypertension	4 (3.7)	2 (1.9)
Dyspnea	3 (2.8)	2 (1.9)
Rash	7 (6.5)	1 (<1)
Bilirubin elevated	7 (6.5)	1 (<1)
Alkaline phosphatase increased	5 (4.7)	1 (<1)
Creatinine phosphokinase increased	2 (1.9)	1 (<1)
Anemia	1 (<1)	1 (<1)
Angioedema	1 (<1)	1 (<1)
Fluid retention	1 (<1)	1 (<1)
Hyperparathyroidism	1 (<1)	1 (<1)
Hypocalcemia	1 (<1)	1 (<1)
Hyponatremia	1 (<1)	1 (<1)
Increased international normalized ratio	1 (<1)	1 (<1)
Malaise	1 (<1)	1 (<1)
Altered mental status	1 (<1)	1 (<1)
Syncope	1 (<1)	1 (<1)

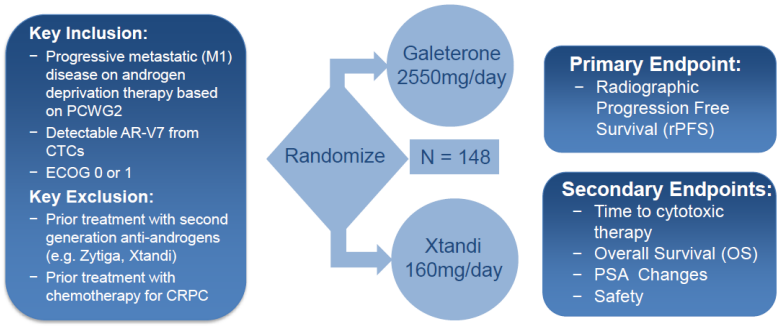
Sources: Company reports, 2014 EORTC-AACR

Galeterone pivotal phase III ARMOR3-SV trial

TKAI plans to initiate a pivotal phase III ARMOR3 trial evaluating the safety and efficacy of galeterone in patients with progressive metastatic (M1) patients in 1H15. The company has finalized the trial design with the FDA. TKAI has also received advice from regulatory agencies in EU and Canada and anticipates that ARMOR3 trial should be sufficient to support approval in these regions as well.

- **Phase III ARMOR3-SV trial design.** ARMOR3-SV is a phase III, randomized, open-label, multicenter, controlled trial comparing galeterone with Xtandi in men expressing AR splice variant-7 mRNA (AR-V7) mCRPC. The patients are naive to the second generation anti-androgen therapies, including Zytiga and Xtandi. Patients also need to be chemotherapy-naive to be enrolled in the trial. The trial targets to enroll approximately 148 patients at over 100 study sites in nine countries including US, Australia, Belgium, Canada, France, Germany, Italy, UK and Spain. It is powered at 90% to detect an 82% increase in median rPFS in the galeterone-treated arm vs. Xtandi-treated arm.

Exhibit 17. Galeterone Phase III Trial Design



Source: Company Reports

The primary efficacy endpoint for the trial is radiographic progression-free survival (rPFS). The secondary endpoints of the trial include time to cytotoxic therapy, overall survival, PSA changes and safety.

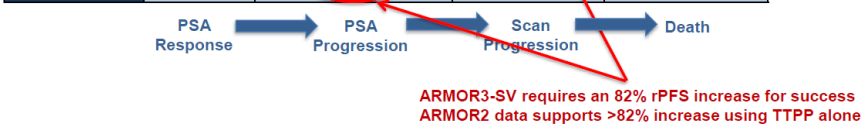
- **We see phase III ARMOR3 trial has a high probability of success**

  We see the trial design (frontline M1 CRPC vs. Xtandi, primary endpoint of rPFS, and a small number of patients n=148) as highly favorable since it requires only a small number of patients, relatively short follow-up time and spares potential negative impact from follow-on therapies (vs. if OS were the primary endpoint).

We believe the phase III trial has a good cushion for success given a high power of 90% to detect an 82% increase in median rPFS between the two arms. The phase II ARMOR2 trial showed a median time to PSA progression (TTPP) of 7.3 months and a PSA50 response rate of 86%. As a comparison, the Johns Hopkins study showed that Xtandi had a PSA50 response rate of 0% and rPFS of 2.1 months in AR-V7 positive patients. Although we caution investors the limitation of comparing results cross different trials, since the patient polution in the two studies differ (treatment naive in ARMOR2 trial vs. previously treated patients in Xtandi-treated patients in the Johns Hopkins trial), we still see the phase III trial has sufficient room for success, given the 247% improvement of galeterone (using TTPP) vs. Xtandi rPFS (7.3 months vs. 2.1 months) and that we expect PSA progression should come earlier than rPFS (i.e. rPFS should be longer than TTPP).

Exhibit 18. Galeterone in C-terminal Loss Patients Show Higher PSA50 Rates and Longer Time to PSA Progression

Treatment	PSA50	PSA Progression (mos)	rPFS (mos)	OS (mos) (95% CI)
Xtandi in AR-V7+ [1] (n=12 patients with AR-V7+ disease)	0%	1.4 (PSA Progression Free Survival)	2.1	7.4 (3.9–NR)
ARMOR2 Galeterone in C-terminal Loss (n=7) [2]	86%	7.3 (Time to PSA Progression)	UNK	UNK



ARMOR3-SV requires an 82% rPFS increase for success
ARMOR2 data supports >82% increase using TTPP alone

Source: Company reports

Galeterone Addresses a Large Market with Unmet Need

We believe galeterone can address a sizeable unmet medical need for which no current available therapies are expected to be effective. We project galeterone to achieve US peak sales of ~$1.4B by 2025 (Exhibit 19). In our model, we factor in potential approval of galeterone 2017 in frontline M1 CRPC and market launch in 2018. We believe that, once approved, the likelihood for off-label use in AR-V7 positive patients post-Xtandi and Zytiga treatment is high given the lack of effective therapy.

The prevalence of AR-V7+ is estimated to be between 12% and mid-20% in the M1 CRPC patients before treatment of Xtandi and Zytiga. However, the prevalence tends to increase significantly following subsequent treatment lines (25%, 51% and 67% in post-Zytiga, post Xtandi and post both treatments, respectively). We believe galeterone has significant potential in the resistant subset since existing therapies are not effective. Additionally, we see very little competitive risk since no other drug is currently in clinical development targeting the same patient population (to the best of our knowledge).

We project galeterone US peak sales of ~$1.4B in 2025, which include sales in the frontline M1 CRPC patients of $800M (peak penetration of 75%) and sales in AR-V7 positive patients post-Xtandi and Zytiga treatment of $567M (peak penetration of 50%).

Exhibit 19. Revenue Projections of Galeterone in the US

U.S. Pre-Zytiga and Xtandi M1 CRPC Market	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Prostate cancer incidence	263,423	270,008	276,758	283,677	290,769	298,039	305,490	313,127
% need hormonal therapy	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
PC diagnosed with local disease	79,027	81,002	83,028	85,103	87,231	89,412	91,647	93,938
% progressing to metastatic CRPC	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*
PC patients progressing to mCRPC	59,270	60,752	62,271	63,827	65,423	67,059	68,735	70,454
% with asymtomatic/minimal symtoms	*93%*	*93%*	*93%*	*93%*	*93%*	*93%*	*93%*	*93%*
# of asym / minimally symptomatic CRPC	55,121	56,499	57,912	59,359	60,843	62,365	63,924	65,522
% with AR-V7+ tumor	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
# frontline M1 patients with AR-V7+ tumor	8,268	8,475	8,687	8,904	9,127	9,355	9,589	9,828
Galeterone penetration	*6%*	*18%*	*36%*	*54%*	*65%*	*75%*	*75%*	*75%*
# of patients treated with galeterone	496.09	1,525	3,127	4,808	5,914	7,016	7,191	7,371
Galeterone annual treatment cost in frontline M1 CRPC	99,167	102,142	105,206	108,362	105,206	108,362	111,613	108,362
Galeterone sales in frontline M1 CRPC	**49,196**	**155,815**	**329,003**	**521,018**	**622,186**	**760,270**	**802,655**	**798,759**
U.S. Post Zytiga and Xtandi M1 CRPC Market	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**
PC patients progressing to CRPC	59,270	60,752	62,271	63,827	65,423	67,059	68,735	70,454
% treated with both Xtandi and Zytiga	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*
# CRPC who have failed both Xtandi and Zytiga	23,708	24,301	24,908	25,531	26,169	26,823	27,494	28,181
% of patients with AR-V7+ tumor	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*
# post-Zytiga/Xtandi CRPC patients eligible for galeterone	15,410	15,795	16,190	16,595	17,010	17,435	17,871	18,318
Galeterone penetration	*2%*	*8%*	*16%*	*24%*	*29%*	*45%*	*50%*	*50%*
# of patients treated with galeterone	308.20	1,264	2,590	3,983	4,899	7,846	8,936	9,159
Galeterone pricing/year	85,000	87,550	90,177	92,882	90,177	92,882	95,668	92,882
Treatment duration (months)	8	8	8	8	8	8	8	8
Galeterone annual treatment cost in the post Zytiga/Xtand	56,667	58,367	60,118	61,921	60,118	61,921	63,779	61,921
Galeterone sales in post-Zytiga/Xtandi M1 CRPC	**17,465**	**73,754**	**155,732**	**246,622**	**294,509**	**485,825**	**569,900**	**567,134**
Total U.S. sales in M1 CRPC	**66,661**	**229,569**	**484,736**	**767,639**	**916,696**	**1,246,095**	**1,372,555**	**1,365,892**

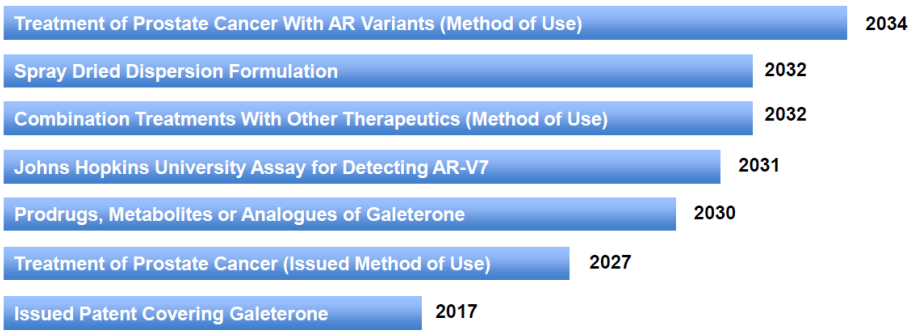
Source: Oppenheimer & Co. Inc. Research

We derive galeterone risk-adjusted NPV of ~$923M by using a probability of success of 75%, a revenue multiple of 5x on our 2023 projected galeterone risk-adjusted sales, and a discount rate of 30%. We also assume TKAI finds a partner to market galeterone in ex-US market. We assume 2023 ex-US sales of ~$787M (or approximately 60% of the US sales in 2023), royalty rate of 20% and a multiple on royalties of 10x.

Intellectual Property

TKAI owns a broad patent portfolio related to galeterone. As of February 28, 2015, the company owned two issued US patents, nine US provisional and non-provisional patent applications, one issued foreign patent and 35 foreign applications in the galeterone patent portfolio. It also has rights under the license agreement with UMB to five issued US patents and 70 issued foreign patents as well as three US patent applications and 8 foreign applications. Additionally, TKAI also own rights under a license agreement with Johns Hopkins to two US patent applications and two foreign patent applications. The owned and licensed patent and patent applications, if issued, are expected to expire on various dates from 2017 through 2034, without taking into account any possible patent term extensions.

Exhibit 20: Galeterone Intellectual Property Timeline



Source: Oppenheimer & Co. Research

Key Licensing Agreement

License agreement with University of Maryland, Baltimore

In May 2006, TKAI in-licensed exclusive worldwide rights to galeterone from the University of Maryland, Baltimore (UMB). The licensing agreement has since been updated and amended. The key components of the financial terms include:

- Annual maintenance fee of $10,000 until the first commercial sale;
- A milestone payment of $50,000 for each additional IND submission;
- A milestone payment of $100,000 upon each NDA approval by the FDA;
- Royalty payment in low-single digit royalty rate (minimum of $50,000/year);
- 10% of all non-royalty sublicense income received from sublicensees if galeterone is sublicensed to third parties.

Agreement with Johns Hopkins University

In January 2015, TKAI entered into an agreement with the Johns Hopkins University for the development of a companion diagnostic to determine the AR-V7 status of patients with CRPC for use with galeterone in the planned pivotal phase III trial. Under the agreement, TKAI has obtained an exclusive, worldwide license from the Johns Hopkins University to patent applications and know-how covering an assay that has been used to determine the AR-V7 status of prostate cancer patients.

Agreement with Qiagen

In 2015, TKAI entered into an agreement with Qiagen N.V. (QGEN, Not Rated) under which Qiagen will develop a non-invasive companion diagnostic utilizing an array of novel technologies for use with galeterone. The two companies also expanded the collaboration recently. Under the expanded agreement, TKAI will receive the exclusive right from Qiagen to its newly acquired circulating tumor cell (CTC) enrichment technology for use with galeterone, which will be incorporated into the companion diagnostic already under development by Qiagen. Development of an AR-V7 companion diagnostic for use with galeterone has been initiated since October 2014. Qiagen's newly acquired CTC technology was utilized in the AR-V7 assay methods developed by the Johns Hopkins University licensed by TKAI in January 2015.

Balance Sheet

TKAI ended 2014 with approximately $105M in cash, cash equivalents, and marketable securities, which should be sufficient to fund operation through top-line ARMOR3 data in 2H16.

Management Profile

Key Officer	Position	Biography
Jodie Morrison	President and CEO	Jodie has served as president and CEO at Tokai and as a member of the board of directors since March 2013. Prior to her appointment, Jodie served as both the company's COO and head of clinical affairs over the seven preceding years. Throughout her tenure at Tokai, Jodie has led the company's operational management and galeterone prostate cancer development program. Prior to joining Tokai, Jodie was director of clinical operations and medical affairs at Dyax Corporation. During her tenure at Dyax, she built and led the clinical development teams for Kalbitor (hereditary angioedema) and DX-88 (cardiothoracic surgery), and oversaw the Kalbitor clinical trials that ultimately led to its marketing approval. Prior to joining Dyax, she held clinical management positions at both Curis, Inc. and at Diacrin, Inc. Jodie received a B.A. in neuroscience from Mount Holyoke College, her business training through the Greater Boston Executive Program at MIT Sloan School of Management and her clinical research certification from Boston University School of Medicine.
Karen Ferrante, MD	CMO and Head of R&D	Karen has served as head of R&D and CMO at Tokai since April 2014. Prior to Tokai, she served as oncology therapeutic area head for Takeda Pharmaceuticals and Takeda Cambridge, USA site head. Prior to that, Karen held senior positions at Millennium Pharmaceuticals and its parent company, Takeda Pharmaceuticals including her role as CMO and a head of R&D for Millennium. From 1999 to 2007, she held positions of increasing responsibility at Pfizer Global Research & Development, culminating as vice president and therapeutic area clinical leader in oncology development. Karen began her career in the pharmaceutical industry as associate director of clinical oncology at Bristol-Myers Squibb Company. For more than a decade prior, she was at the New England Deaconess Hospital in Boston (Beth Israel Deaconess), where she completed her internship and residency in internal medicine followed by her fellowship in hematology and oncology. While at the Beth Israel Deaconess Hospital, she served as instructor, clinical instructor and clinical fellow in medicine at the Harvard Medical School. Karen has been an author of a number of peer-reviewed papers in the field of oncology, an active participant in academic and professional associations and symposia, is the holder of several patents and serves as a member of the board of Progenics Pharmaceuticals. Karen holds a B.S. in chemistry and biology from Providence College and an M.D. from Georgetown University.
Lee Kalowski, MBA	CFO	Lee has served as CFO at Tokai since September 2014. Prior to joining Tokai, he served as a vice president in global biotechnology equity research at Credit Suisse. In this role, Lee served as a senior research analyst covering the biotechnology industry, including numerous companies globally in the prostate cancer therapeutic area. Prior to Credit Suisse, Lee worked at Johnson & Johnson in mergers & acquisitions in the pharmaceutical group, where he was involved in the analysis and execution of several completed transactions, and in global pharmaceutical equity research at Sanford C. Bernstein and Prudential Equity Group. Lee holds a B.A., Phi Beta Kappa, in biology and economics, from Union College and an M.B.A. in finance and health care management from the Wharton School, University of Pennsylvania.
John McBride, MS, MBA	COO	John has served as chief operating officer at Tokai since February 2014. Prior to joining Tokai, he founded and served as president of Alliance Life Science Advisors, Inc., a consulting firm focused on assisting life science companies with strategic planning, business development and financing projects. Prior to that, John was executive vice president and chief operating officer of Gloucester pharmaceuticals, Inc. where he was responsible for the company's business development, finance, administrative and manufacturing functions. He has also served as global head of oncology licensing at Pharmacia Corporation; executive vice president, business operations and chief financial officer at CytoTherapeutics, Inc.; vice president, business development and treasurer at Phytera, Inc.; vice president, commercial development at Sparta Pharmaceuticals, Inc.; and vice president, business development at U.S. Bioscience, Inc. John holds a B.S. in biochemistry and an M.S. in chemical engineering from the University of Wisconsin and an M.B.A. from the Wharton School, University of Pennsylvania.
Dan Dransfield, PhD	VP, Head of Translational Medicine	Dan served as the VP, Head of Translational Medicine since August 2014. Prior to Tokai, Dan held vice president positions in discovery research, translational medicine and kinase biology at ArQulw since 2012, where he supervised multiple teams of scientists that evaluated therapeutic candidates, shaping the company's clinical programs and development strategy. Prior to his positions at ArQule, Dan spent 11 years at Dyax Corporation in roles of increasing responsibility, culminating as vice president of cell biology and translational research. Prior to Dyax, he worked for nearly a decade in various instructor and scientist roles at the Institute of Molecular Medicine & Genetics, Medical College of Georgia. Dr. Dransfield has authored a number of peer-reviewed papers, is an active participant in professional oncology associations and is the holder of several patents. He has a B.S. in biology from The Catholic University of America and a Ph.D. from Tufts University.

Stock prices of other companies mentioned in this report (as of 5/8/15):

Johnson Johnson (JNJ-NYSE, $101.47, Not Covered)
Medivation (MDVN-NYSE, $123.65, Not Covered)
Qiagen (QGEN-NYSE, $24.72, Not Covered)

Financial Models

Tokai Pharmaceuticals, Inc.

Income Statement & Financial Projections

(Figures in thousands, except per share items)

	2012A	2013A	1H14A	3Q14A	4Q14A	2014A	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E
Revenue												
Operating expenses:												
Research and development	7,370	12,201	7,948	2,825	3,804	14,577	3,950	4,800	7,500	8,300	24,550	36,000
General and administrative	2,279	3,548	2,829	3,599	2,457	8,885	2,800	2,950	3,100	3,300	12,150	14,500
Total operating expenses	**9,649**	**15,749**	**10,777**	**6,424**	**6,261**	**23,462**	**6,750**	**7,750**	**10,600**	**11,600**	**36,700**	**50,500**
Loss from operations	**(9,649)**	**(15,749)**	**(10,777)**	**(6,424)**	**(6,261)**	**(23,462)**	**(6,750)**	**(7,750)**	**(10,600)**	**(11,600)**	**(36,700)**	**(50,500)**
Other income		24	79	34	53	166	50	43	34	30	157	100
Net loss and comprehensive loss	**(9,649)**	**(15,725)**	**(10,698)**	**(6,390)**	**(6,208)**	**(23,296)**	**(6,700)**	**(7,707)**	**(10,566)**	**(11,570)**	**(36,543)**	**(50,400)**
Accretion of redeemable convertible preferred stock to redemption value	(34)	(94)										
Net loss attributable to common stockholders	(9,683)	(15,819)	(10,698)	(6,390)	(6,208)	(23,296)	(6,700)	(7,707)	(10,566)	(11,570)	(36,543)	(50,400)
EPS, basic and diluted	($31.1)	($38.0)	($2.05)	($2.71)	($0.28)	($3.60)	$ (0.30)	$ (0.34)	$ (0.47)	$ (0.51)	$ (1.62)	$ (2.15)
Common shares outstanding, basic and diluted	311,474.0	416,037.0	5,215	2,357	22,329	6,469	22,441	22,553	22,666	22,779	22,610	23,462

Source: Company reports & Oppenheimer & Co. Research

Tokai Pharmaceuticals, Inc.

Balance Sheet

(Figures in thousands)

	2013	2014
Assets		
Current assets:		
Cash and cash equivalents	$31,753	$105,256
Prepaid expenses and other current assets	$425	$2,255
Total current assets	**$32,178**	**$107,511**
Property and equipment, net	$29	$33
Deferred offering costs	$30	
Restricted cash	$50	$200
Total assets	**$32,287**	**$107,744**
Liabilities, Redeemable Convertible Preferred and Stockholders' Equity		
Current liabilities:		
Accounts payable	$5	$765
Accrued expenses	$2,204	$3,478
Total current liabilities	**$2,209**	**$4,243**
Total liabilities	**$2,209**	**$4,243**
Commitments and contingencies (Note 9)		
Redeemable convertible preferred stock (Series A, B-1, B-2, C, D-1, D-2	$85,345	
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value;		
Common stock, $0.001 par value;		$22
Additional paid-in capital	$7,788	$189,830
Accumulated deficit	($63,055)	($86,351)
Total stockholders' equity (deficit)	**($55,267)**	**$103,501**
Total liabilities, redeemable convertible preferred stock and stockhol	**$32,287**	**$107,744**

Source: Company reports & Oppenheimer & Co. Research

Tokai Pharmaceuticals, Inc.

Cash Flow Statement

(Figures in thousands)

	2012	2013	2014
Operating activities:			
Net loss	**($9,649)**	**($15,725)**	**($23,296)**
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	$210	$238	$2,108
Depreciation expense	$9	$10	$21
Release of reserve for loan to former advisor			($158)
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	$139	($190)	($1,830)
Accounts payable	($119)	($759)	$760
Accrued expenses	$77	$950	$1,274
Net cash used in operating activities	**($9,333)**	**($15,476)**	**($21,121)**
Investing activities:			
Purchases of property and equipment	($8)	($23)	($25)
Change in restricted cash		($30)	($150)
Net cash used in investing activities	**($8)**	**($53)**	**($175)**
Financing activities:			
Net proceeds from IPO			$97,929
Payments of initial public offering costs		($30)	($3,304)
Proceeds from issuance of redeemable convertible preferred stock, net c	$18,775	$35,406	
Repayment of notes receivable			$158
Proceeds from exercise of common stock options	$4	$215	$16
Net cash provided by financing activities	$18,779	$35,591	$94,799
Net increase in cash and cash equivalents	**$9,438**	**$20,062**	**$73,503**
Cash and cash equivalents at beginning of period	$2,253	$11,691	$31,753
Cash and cash equivalents at end of period	**$11,691**	**$31,753**	**$105,256**
Supplemental disclosure of non-cash investing and financing activities:			
Accretion of redeemable convertible preferred stock to redemption value	$34	$94	
Conversion of redeemable convertible preferred stock to common stock			($85,345)
Conversion of convertible promissory notes and accrued interest and adv	$141		

Source: Company reports & Oppenheimer & Co. Research

Investment Thesis

TKAI's flagship compound galeterone addresses a clear unmet medical need in prostate cancer, i.e. patients with tumor-expressing androgen receptor (AR) split variants (in particular AR-V7) for whom recently approved novel agents such as Zytiga and Xtandi are not expected to work potentially due to the loss of ligand binding domain (LBD). We view TKAI as a highly favorable biotech name, given a clear pathway for approval, a high probability of phase III success, large market opportunity and no foreseeable competition.

Price Target Calculation

Our 12- to 18-month price target of $38 is primarily based on the risk-adjusted NPV of galeterone of ~$923M (~$38/share). We project galeterone 2023 US sales of $1.2B and ex-US sales of ~$748M (royalty rate of ~20% in ex-US sales). We use a biotech typical revenue multiple of 5x, royalty multiple of 10x, a probability of success of 75%, discount rate of 30% (which reflects the development stage of the company) to derive the risk-adjusted NPV of galeterone.

Key Risks to Price Target

We view clinical risks associated with galeterone as the main risk for TKAI. Other risks include regulatory risks, financing risk, commercialization risk.

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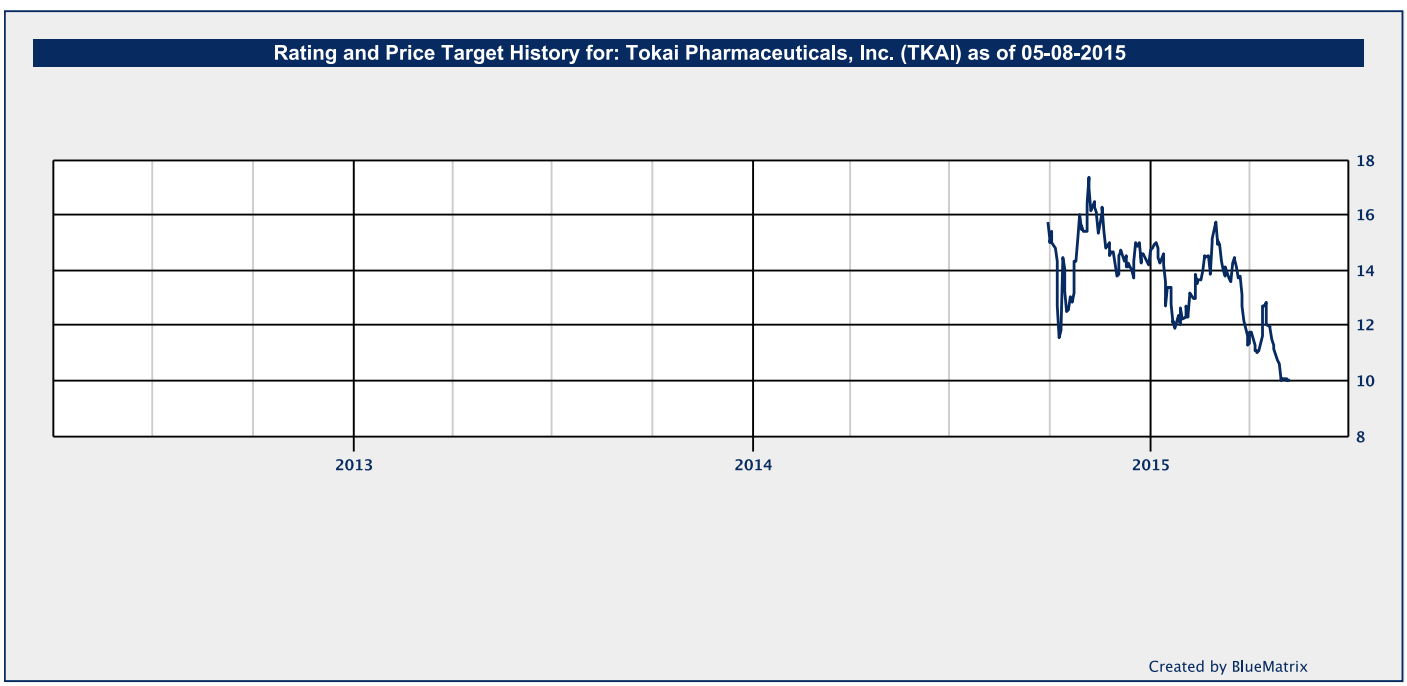

All price targets displayed in the chart above are for a 12- to- 18-month period. Prior to March 30, 2004, Oppenheimer & Co. Inc. used 6-, 12-, 12- to 18-, and 12- to 24-month price targets and ranges. For more information about target price histories, please write to Oppenheimer & Co. Inc., 85 Broad Street, New York, NY 10004, Attention: Equity Research Department, Business Manager.

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Distribution of Ratings/IB Services Firmwide

			IB Serv/Past 12 Mos.	
Rating	Count	Percent	Count	Percent
OUTPERFORM [O]	323	55.69	147	45.51
PERFORM [P]	249	42.93	93	37.35
UNDERPERFORM [U]	8	1.38	2	25.00

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