These advances should have reduced uncertainty concerning which patients are appropriate for therapy and speed up the claims process, respectively, and Dendreon notes that reimbursement concerns are now beginning to fade.

…But Demand May Be More To Blame

As of Q2:11, Dendreon indicated that Provenge's launch was in "full swing" with utilization limited only by how fast physicians could prescribe the drug. Dendreon ended Q1:11 with 135 "active" Provenge accounts, and the company guided to 225 active accounts by the end of Q2, and roughly 500 active accounts by year end. Dendreon exceeded its guidance for opening new accounts during Q2 with more than 265 sites, but the average number of patients treated per center (0.8/month) was well below expectations (1-2/month). As a result, Dendreon missed its guidance for Q2 sales (reported sales of $49MM versus a target of $54-60MM) and withdrew its 2011 sales projection. At the end of Q4:11 and Q1:12, the number of sites infusing Provenge increased to 595 and 723, respectively, but with similarly low numbers of average patients per site. In our view, visibility into identifying patients who are suitable for Provenge is lacking.

There are several factors that could explain the lower than expected demand. First, patients with minimally symptomatic PRCA are not always closely followed by their physicians, and clinical practices have a difficult time recalling such patients in order to recommend a therapy like Provenge. Second, patients rapidly progress into and out of a metastatic, asymptomatic CRPC state of disease. Unless patients are caught while asymptomatic or minimally symptomatic, it may be too late to offer Provenge. Lastly, JNJ's Zytiga may be gaining traction in Provenge's market. Checks with consultants indicate increasing off-label prescribing in pre-chemotherapy patients, and although Zytiga's mechanism is viewed as complementary to Provenge, it is clear that some physicians are satisfied giving only Zytiga based upon its convenience (oral), rapid onset, and symptomatic benefits. Provenge may also face future competition from Medivation's enzalutamide, which is also being tested in metastatic CRPC. Our consultants expect earlier use of both Zytiga and enzalutamide to pressure Provenge, but overall expect sales growth to "stagnate" as opposed to decline.

What Is The Potential Opportunity For Provenge In The U.S.?

According to the American Cancer Society, approximately 217K new cases of prostate cancer were diagnosed in the U.S. in 2010, with an estimated 32K deaths. Patients' disease is usually controlled for many years on anti-androgen therapies, eventually becoming refractory, or "castrate-resistant". We estimate that roughly 30-35K patients in the U.S. develop metastatic CRPC each year.

According to consultants, the large majority (80-90%) of patients with metastatic CRPC initially have few or no symptoms. Most CRPC patients are usually treated initially with a second-line hormonal agent (e.g. Casodex, ketoconazole, estrogens, steroids), and chemotherapy with Taxotere is usually delayed until patients develop symptomatic metastatic disease. Our consultants estimate that about 16K patients with CRPC are treated annually with Taxotere in the U.S., representing about half of all U.S. metastatic CRPC patients.

In general, physicians expect to administer Provenge prior to chemotherapy, based on their view that Provenge takes time to manifest its effect, and because many patients refuse chemotherapy. We note that Dendreon's marketing campaign is

Astellas has a strong commercial presence in urology, selling Flomax for benign prostatic hyperplasia (BPH) and Vesicare for overactive bladder on a global basis, so should be a good sponsor for enzalutamide in urology circles.

JNJ's Zytiga Is The Main Competitor

There are a number of new entrants in the prostate cancer (PRCA) marketplace (Zytiga, carbazitaxel, Provenge) and several promising therapies waiting in the wings (Alpharadin, cabozantinib). However, JNJ's Zytiga appears to be the main initial threat to enzalutamide given their related mechanisms of action and potential to be used in patients who are not yet truly androgen independent.

JNJ's Zytiga (abiraterone) demonstrated a 3.9 month median overall survival benefit at the interim analysis and a 4.6 month benefit at the final analysis Study 301 (chemotherapy-refractory CRPC). Patients in the abiraterone/prednisone arm had a median survival of 14.8 months, vs. 10.9 months for the control arm (HR 0.65; p<0.0001). Zytiga also improved time to disease progression (10.2 vs. 6.6 months; p<0.0001). Hence the efficacy of Zytiga and MDV3011 appears comparable.

In March, Zytiga's pivotal COU-AA-302 trial in chemotherapy-naive prostate cancer patients was halted due to convincing efficacy of Zytiga relative to the standard-of-care control arm. The interim data through December 2011 showed a statistically significant improvement in radiographic progression-free survival (rPFS) in patients receiving Zytiga plus prednisone compared to the placebo plus prednisone in the control group (p<0.0001). The median rPFS in the control group was 8.3 months, but as of the December 2011 interim look, median rPFS had not yet been reached in the Zytiga treatment group (n=150 progression events in the Zytiga treatment group vs. 251 in the control group; HR = 0.43; 95% CI = [0.35, 0.52]; p<0.0001). Zytiga showed a strong trend in favor of an overall survival benefit, but did not achieve statistical significance on OS at the interim look. (HR=0.75, p=0.0097 vs. prespecified p-value of 0.0008).

Zytiga works through a similar anti-androgen-based mechanism, and at this stage there is little data on its combinability with enzalutamide. There is also some anecdotal evidence to suggest that sequential therapy may not be ideal. In other words, once a patient becomes resistant to one, he is more likely resistant to the other. As a result, it was important that enzalutamide produce survival data that are at least on par with Zytiga, allowing Medivation and Astellas to position enzalutamide as a therapy that could be used ahead of Zytiga.

Zytiga was approved by the FDA in April 2011 and EMA in September 2011. JNJ posted $301MM WW sales in 2011. Enzalutamide's major advantage relative to Zytiga appears to be its superior tolerability. Zytiga requires co-administration of prednisone, a steroid which over time is difficult to tolerate. This is less of an issue in the post-chemotherapy setting where many men receive prednisone with Taxotere and never come off. However, in the pre-chemotherapy setting, where patients could stay on drug for multiple years, enzalutamide could have a natural advantage. Enzalutamide (once daily, no food restrictions) may also be somewhat more convenient to administer than Zytiga (BID, with food).

Consultants Give Enzalutamide The Nod Over Zytiga

In May we hosted a physician consultanting call on prostate cancer. The two clear "winners" from our call were MDVN's enzalutamide and JNJ's abiraterone (Zytiga).

Our specialists view JNJ's Zytiga (abiraterone) and Medivation's enzalutamide as having comparable efficacy in the treatment of post-chemotherapy CRPC. However, they noted that the two drugs have differences in their activity on androgens and that a differential mechanism is reflected in the side-effect profiles. While both drugs are viewed as far safer than chemotherapy, clinicians indicated that enzalutamide may have a modestly better side-effect profile, terming it "amazingly clean", and suggesting its low seizure risk was a bit more acceptable than Zytiga's requirement for concomitant steroid dosing. In terms of seizures, doctors indicated that those observed were mild, and not necessarily all drug related. They think the important thing is not to use enzalutamide in combination with other agents that lower seizure risk. One of our specialists has been dosing Zytiga with a lower ("sub-physiologic") dose of prednisone (5mg QD rather than 5mg BID), and has seen no change in the side-effects related to Zytiga but an improvement in the prednisone-related side effects. Still this consultant believes that enzalutamide's overall tolerability profile remains superior to that of Zytiga.

Comparison Between MDVN's Enzalutamide And JNJ's Abiraterone

MDV3100 VS. ZYTIGA POST-CHEMO CRPC COMPARISON

Key Endpoints Measured	MDV3100 160mg QD	placebo	p-values (HR 95% CI)	Zytiga 1,000mg QD + 5mg prednisone BID	placebo + prednisone	p-values (HR 95% CI)
	(n=799)	(n=400)		(n=797)	(n=398)	
Overall survival (OS)	**18.4 months**	**13.6 months**	**p<0.0001 (HR=0.631)**	**15.8 months**	**11.2 months**	**p<0.0001 (HR=0.74)**
net improvement in OS vs. PBO	**4.8 months**			**4.6 months**		
radiographic PFS (rPFS)	8.3 months	2.9 months	p<0.0001 (HR=0.404)	5.6 months	3.6 months	p<0.001
time to PSA progression (TTPP)	8.3 months	3.0 months	p<0.0001 (HR=0.249)	10.2 months	6.6 months	p<0.001
soft tissue/PSA response rate	28.9%	3.8%	p<0.001	29.1%	5.5%	p<0.001
PSA declines of ≥50%	54.0%	1.5%	p<0.0001			
PSA declines of ≥90%	24.8%	0.9%	p<0.0001			
Safety Profile						
Common Grade 3 or greater AEs:	45.3%	53.1%				
seizure incidence	0.6% (5 patients)	0.0%		0.0% (0 patients)		
fatigue	6.3%	7.3%		---	---	
cardiac disorders	0.9%	2.0%		---	---	
myocardial infarction	0.3%	0.5%		---	---	
liver function test abnormalities	0.4%	0.8%		---	---	
joint swelling/discomfort	---	---		29.5%	4.2%	
muscle discomfort	---	---		26.2%	3.0%	
edema	---	---		26.7%	1.9%	
hypertension	---	---		8.5%	1.3%	
diarrhea	---	---		17.6%	0.6%	
dyspepsia	---	---		6.1%	0.0%	
urinary tract infections	---	---		11.5%	2.1%	
upper respiratory tract infections	---	---		5.4%	0.0%	
arrhythmias	---	---		7.2%	1.1%	
chest pain or discomfort	---	---		3.8%	0.5%	
cardiac failure	---	---		2.3%	1.9%	
Label Warnings	TBD (currently seeking approval in post-chemo CRPC)			- mineralocorticoid excess - adrenocortical insufficiency - hepatotoxicity - food effect		
Pregnancy Category	TBD (currently seeking approval in post-chemo CRPC)			Category X (not indicated for use in pregnant women)		

Source: Cowen and Company; Company Data

Source: Cowen and Company, ASCO Abstract 2010

Post-Chemotherapy Setting Is Relatively Modest

Between 30-35K U.S. patients succumb to metastatic PRCA each year. Roughly 60% of these patients are believed to receive Taxotere and are therefore likely to be eligible for enzalutamide. We assume that Zytiga's entrenched status and enzalutamide's less differentiated profile in this setting will allow these drugs to share this market roughly equally. However, the more successful enzalutamide becomes in the much larger pre-chemotherapy setting (see below), the less likely it will be used in post-chemotherapy patients as patients are unlikely to get two courses of the drug. We

model U.S. sales of $75MM in 2013 and $225MM in 2017 in the post-chemotherapy CRPC setting. We view Europe as a similar sized opportunity on which we estimate MDVN will receive escalating royalties in the 15-22% range.

U.S. Post Chemotherapy Revenue Model

United States	2013	2014	2015	2016	2017
Post-chemotherapy Setting					
Incidence of metastatic CRPC	31.0	31.3	31.7	32.0	32.4
Penetration of Taxotere	*60%*	*60%*	*60%*	*60%*	*60%*
# patients who receive first-line chemotherapy	18.6	18.8	19.0	19.2	19.4
Penetration of MDV 3100 into second-line	*27%*	*48%*	*37%*	*26%*	*23%*
# patients who receive MDV 3100 post-chemotherapy	5.0	9.0	7.0	5.0	4.5
MDV 3100 price per patient	$50,000	$50,000	$50,000	$50,000	$50,000
MDV3100 sales in post-chemotherapy setting ($MM)	**$250**	**$450**	**$350**	**$250**	**$225**

Source: Cowen and Company

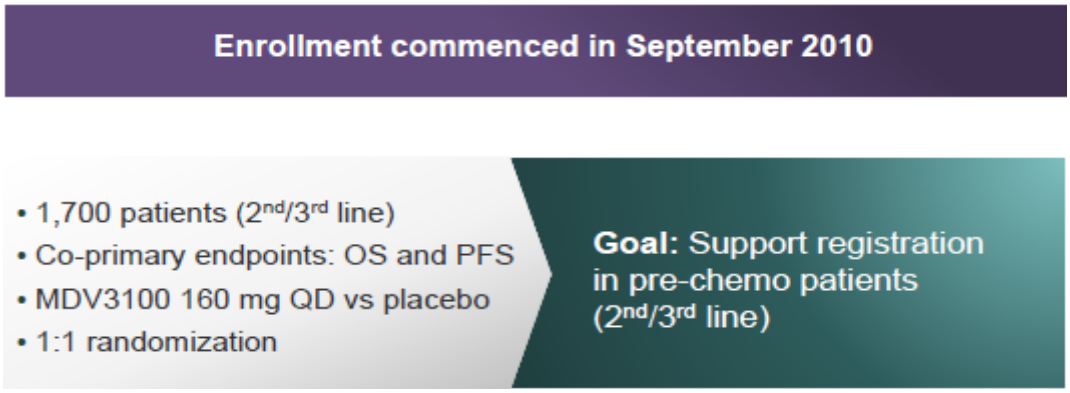
Pre-Chemotherapy Is Where The Money Lies

Many more patients fail androgen deprivation therapy and develop metastatic CRPC each year than receive Taxotere. We estimate the pre-chemotherapy market might be 5x larger than the post chemotherapy market. In theory, both MDV3011 and Zytiga are likely to work in this patient subset. Both drugs rely on the fact that there are several ways through which prostate tumors become resistant to androgen deprivation therapy. These include through the overproduction of adrenal androgens, the development of androgen receptor mutations, amplifications in the androgen receptor, and the outgrowth of cells no longer sensitive to androgens. Neither Zytiga nor enzalutamide will work in patients who harbor tumors that are truly insensitive to androgens. However Zytiga and enzalutamide ought to work in patients who overproduce androgens, or develop androgen receptor mutations/ amplifications that make their cancer cells more sensitive to low concentrations of testosterone for growth.

PREVAIL Fully Enrolled

In September 2010, Astellas and Medivation initiated the Phase III PREVAIL trial evaluating enzalutamide in CRPC patients who are chemotherapy naïve. PREVAIL is testing the hypothesis that enzalutamide improves OS and PFS in these patients. In June 2012 Medivation announced that this trial is fully enrolled. PREVAIL is modeled off Zytiga's Study 302 (for which JNJ received an SPA), but is designed to enroll more patients (1,700 vs. 1,000). The inclusion of more patients could allow events to accrue faster, enabling Medivation and Astellas to close some of the gap in timing. JNJ's Study 302 began in April 2009.

PREVAIL Trial Design



Source: Medivation

The trial costs for PREVAIL will be allocated to Medivation and Astellas in the same proportion as the AFFIRM trial (roughly one third : two thirds). The PREVAIL study is enrolling patients in North America, Europe, Australia, and Israel. The co-primary endpoints of the study are overall survival and progression-free survival (PFS). The secondary endpoints in the PREVAIL study include time to first skeletal-related event and time to initiation of chemotherapy.

We Have High Expectations For Enzalutamide In Pre-Chemotherapy

Biologically there appears to be limited differences between a CRPC patient who has failed chemotherapy and one who has not. Moreover, enzalutamide's Phase I/II experience suggests the drug is highly active in pre-chemotherapy patients. In addition, as noted above, pre-chemotherapy is the setting in which enzalutamide's tolerability advantages relative to Zytiga could have the most benefit. Lastly, there is some scientific basis to support why enzalutamide may have greater efficacy relative to Zytiga in this setting (though in the end, the proof will be in the pudding).

While Phase III data in the pre-chemotherapy setting are unlikely before 2013 or 2014, we are comfortable adding significant estimates for enzalutamide in pre-chemotherapy patients to our model. At peak, we believe U.S. sales of enzalutamide in this setting could approach $1.5B. We also model ex-U.S. sales of nearly $1.5B in this setting.

U.S. Pre Chemotherapy Revenue Model

United States	2013	2014	2015	2016	2017
Pre-chemotherapy setting					
# patients on hormonal therapy (000)	675.0	682.4	689.9	697.5	705.2
% patients who progress on hormonal therapy	*23%*	*23%*	*23%*	*23%*	*23%*
# patients who fail hormonal therapy	155.3	157.0	158.7	160.4	162.2
% patients who advance to second-line hormonal therapy	*50%*	*50%*	*51%*	*53%*	*55%*
# patients who receive second-line hormonal therapy	77.6	78.5	80.9	85.0	89.2
Penetration of MDV 3100 into second-line hormonal therapy	*1%*	*1.6%*	*7%*	*11%*	*13%*
# patients who receive MDV 3100 in pre-chemotherapy setting	0.6	1.3	5.6	9.4	11.3
MDV3100 price per patient	$80,000	$80,000	$80,000	$80,000	$80,000
MDV3100 sales in HRPC ($MM)	**$50**	**$100**	**$450**	**$750**	**$900**

Source: Cowen and Company (All figures estimated.)