

A Transforming Time for Prostate Cancer Therapies

Initiating Coverage of Key Biotechnology Companies in the Space: Dendreon, Medivation, and OncoGenex

Over the past few years, the prostate cancer field has witnessed an explosion of development, resulting in a record number of approvals and a full pipeline. This report provides an overview of the disease, market, current treatment paradigm, and competitive development landscape and takes a look into the future. Prostate cancer is the most commonly diagnosed cancer in men. Depending on the state of the disease—local or metastatic, hormone sensitive or castration resistant, asymptomatic or symptomatic—a variety of agents are in use or in development.

Positioning the three biotech players in the prostate cancer space: Dendreon, Medivation, and OncoGenex. Dendreon's Provenge is the first immunotherapy ever approved; it is indicated for frontline therapy for metastatic castration-resistant prostate cancer (mCRPC). We rate Dendreon Underperform with a price target of \$8 based on the following: 1) likely slow uptake of Provenge in the United States as physicians continue to weigh the high cost versus the benefit; 2) strong competition from new agents such as abiraterone and MDV3100, which will likely offer better data and stronger cost-benefit arguments; 3) competition from within the immunotherapy class in 2015 and beyond, such as Prostavac, which is less cumbersome in administration and distribution; and 4) uncertainty around European approval and potentially more limited EU uptake as a result of higher pricing pressure and fiercer competition. We forecast peak sales of \$1.13 billion for Provenge in the United States and \$520 million in Europe, with 60% probability of reaching the market there.

We rate Medivation Outperform with a price target of \$35 because we believe Medivation's MDV3100 (partnered with Astellas) is among the most promising agents, with usefulness not only in the mCRPC setting, but also earlier on the disease continuum in the hormone-sensitive stage. The interim analysis of the Phase III AFFIRM study is expected by year-end 2011; positive data could lead to NDA filing and potential approval in 2012. Our price target is derived from our assumptions of peak sales of \$2.2 billion worldwide and 75% probability for success.

We rate OncoGenex Outperform with a price target of \$21. OncoGenex's lead candidate custirsen (partnered with Teva) is in two Phase III studies, and both are expected to release top-line data during fourth quarter 2012. Custirsen augments the effect of chemotherapeutic agents, and when used in combination, may lead to survival and pain benefits. We forecast \$570 million in peak sales for custirsen and 60% probability for success.

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Healthcare | Biotechnology

September 15, 2011

Basic Report (11-108)

Dendreon Corporation

Stock Rating: **Underperform**
Company Profile: **Aggressive Growth**
Price Target: **\$8**
Symbol: DNDN (NASDAQ)
Price: \$11.90 (52-Wk.: \$9-\$44)

Medivation, Inc.

Stock Rating: **Outperform**
Company Profile: **Aggressive Growth**
Price Target: **\$35**
Symbol: MDVN (NASDAQ)
Price: \$18.91 (52-Wk.: \$11-\$26)

OncoGenex Pharmaceuticals, Inc.

Stock Rating: **Outperform**
Company Profile: **Aggressive Growth**
Price Target: **\$21**
Symbol: OGX1 (NASDAQ)
Price: \$9.99 (52-Wk.: \$9-\$20)

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Prostate Cancer and Its Treatment: An Overview

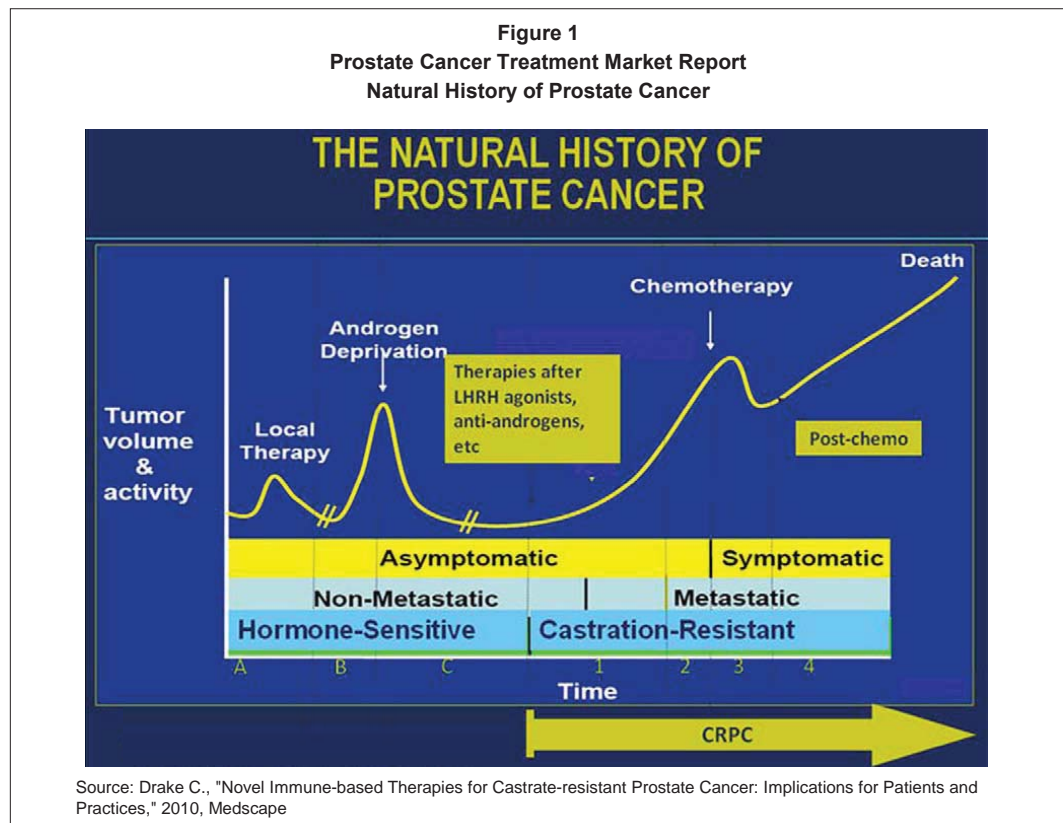
Prostate Cancer Is the Most Commonly Diagnosed Cancer in Men in the United States

Epidemiology. According to the National Cancer Institute, nearly 2.5 million men in the United States have a history of prostate cancer; one in six men will be diagnosed with prostate cancer during his lifetime. It is estimated that in 2010, more than 215,000 new cases of prostate cancer were diagnosed in the United States, accounting for nearly one in every four newly diagnosed cancers among men. Roughly 80% of newly diagnosed patients have the disease localized to the prostate gland, while metastatic prostate cancer accounts for 4%-5% of patients. Localized prostate cancer, if properly treated, has a five-year survival rate of close to 100%; however, 20%-30% of patients eventually relapse after local therapy. When metastatic, the disease invariably becomes fatal, with a five-year survival rate of about 30%. In the United States, around 32,000 men succumbed to the disease in 2010.

Detection and staging. Prostate cancer is detected during medical examination and/or during PSA (prostate-specific antigen) screening. The majority of patients are asymptomatic at the time of diagnosis and symptoms are usually associated with more advanced disease. Prostate cancer is staged from I to IV, with stages I and II classified as localized disease, stage III as locally advanced, and stage IV as metastatic disease (when cancer has already spread to other tissues such as the lymph nodes, bones, and visceral organs, such as liver and lung).

When prostate cancer is suspected, a biopsy is performed and a Gleason score read by a pathologist. The Gleason system is used to grade prostate tumors from 2 to 10, where 10 indicates the most abnormalities.

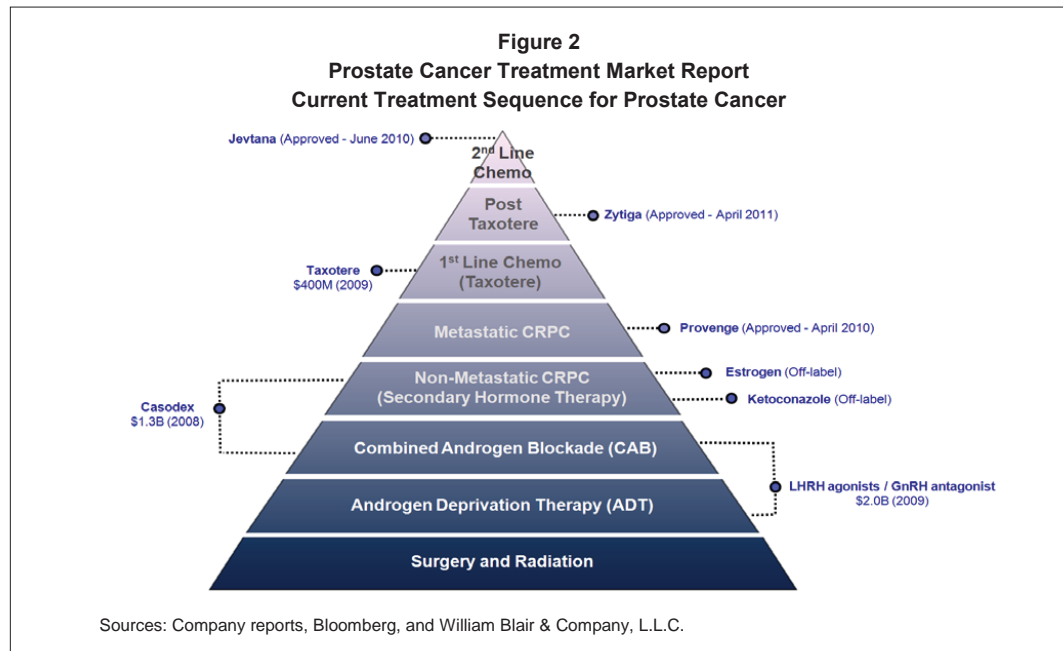
Natural history. The prostate cancer disease-spectrum can be described in a series of states as illustrated in figure 1, defined by the presence or absence of detectable metastases, whether testosterone levels are in the castrate or noncastrate range, and whether the patient is asymptomatic or symptomatic. Each state represents a clinically significant milestone for disease progression and choice of therapies.



Overview of the Current Treatment Sequence

Three new therapies were approved during 2010 and 2011. During the past two years, Provenge (produced by Dendreon), Jevtana (Sanofi), and Zytiga (Johnson & Johnson) gained approval for the treatment of metastatic prostate cancer, and all three therapies demonstrated significant benefits in prolonging overall survival (OS). In contrast, before these three approvals were granted in rapid succession, only Taxotere had been found to prolong survival in prostate cancer patients over the past several decades. With these new therapies and a full pipeline in development as described below, we believe the present time and the next decade will be a transforming period for prostate cancer treatment.

Overview of the current treatment sequence. We summarize the current treatment sequence for prostate cancer in figure 2 and explain in detail each sequence segment below.



Early stage treatment: local therapy of surgery and radiation. For clinically localized diseases, patients are typically segmented into groups based on life expectancy. Individuals with a life expectancy of less than 10 years with low grade or low stage lesions typically undergo active surveillance of their disease, monitoring for changes in PSA levels, symptoms, or Gleason scores to trigger treatment.

For patients with localized disease and a longer life expectancy or for those whose disease has progressed, treatment options include radical prostatectomy, external-beam radiotherapy, and brachytherapy. Radical prostatectomy is the surgical removal of the prostate. External-beam radiotherapy directs a radiation beam from outside the body to the prostate in an effort to destroy the cancerous tissue within the gland. Brachytherapy refers to radiation implants placed directly into the prostate via the guidance of ultrasound or CT imaging.

Castration: Androgen deprivation therapy (ADT) and combined androgen blockade (CAB). Following local treatment, PSA levels are monitored every three to six months; a rising PSA (two to three consecutive increases, or when PSA reaches 10 mg/mL) signals a biochemical recurrence of the disease, suggesting that the disease has either advanced locally or become metastatic. Eventually 20%-30% of patients will have a recurrence following local treatment. At this point, ADT, or castration, is usually initiated. Patients who show elevated levels of PSA or those with a short PSA-DT (PSA-doubling time) may be encouraged to undergo ADT earlier. We note that mechanistically, ADT blocks the signals

from androgens (e.g., testosterone) through the androgen receptors (ARs); active signaling of this pathway is the key driver of increased cancer cell proliferation and progression of the primary tumor.

Patients can undergo two types of ADT: chemical or surgical castration (bilateral orchiectomy). With chemical castration, patients start with a luteinizing hormone-releasing hormone (LHRH) agonist such as Lupron, and over time add an anti-androgen such as Casodex to achieve combined androgen blockade (CAB) (see figures 1 and 2). Bilateral orchiectomy is a surgical procedure to remove both testicles, the major sources of testosterone production. Both ADT methods are effective in reducing androgen levels by 95%, and up to 85% of prostate cancer patients respond to ADT. Unfortunately, the majority of individuals receiving ADT treatment will become nonresponsive to ADTs and progress to castration-resistant prostate cancer (CRPC) over two to three years.

Progression toward CRPC. Although ADT achieves stabilization of disease, over time most patients will progress to CRPC. CRPC refers to tumor progression in spite of castrate levels of androgens (less than 50 ng/mL). Recent data has shown that at this stage, the CRPC still remains androgen driven. Very low levels of androgens, or androgen produced inside the tumors, together with AR gene up-regulation and/or mutations in the AR, continue the signaling for cancer cells to proliferate.

Nonmetastatic CRPC: secondary hormonal therapy using ketoconazole and estrogen. If the cancer progresses despite castrate levels of androgens, the next line of treatment includes use of adrenal enzyme inhibitors, such as ketoconazole, or other anti-androgens, such as estrogens.

Ketoconazole, an anti-fungal agent, is used off-label in CRPC because of its ability to lower testosterone and adrenal androgen levels through its nonspecific inhibition of CYP17, an enzyme involved in the biosynthesis pathway of androgens. DES, a synthetic estrogen, is used in some patients to suppress the production of testosterone by inhibiting the release of LHRH from the hypothalamus.

Metastatic CRPC (mCRPC): Provenge is now frontline before chemotherapy. Metastatic CRPC gradually spreads to the lymph nodes, bone and other organs such as lung and liver. It may not cause symptoms at first, but progressively, bone pain, weight loss, and swelling in legs and feet are manifested. The standard of care for patients who have progressed to the mCRPC stage had been Taxotere until the approval of Provenge in April 2010. Provenge, an autologous cellular immunotherapy, was approved for the treatment of asymptomatic or minimally symptomatic mCRPC; patients on regular pain medication usually would not be candidates for Provenge. The largest randomized Phase III study for Provenge, IMPACT, produced a statistically significant improvement in overall survival (OS) of 4.1 months when compared with placebo (hazard ratio=0.759), and earlier studies demonstrated similar results.

Xgeva (denosumab, Amgen) is indicated for prevention of skeletal-related events, such as fractures, in patients with bone metastases from solid tumors, including late stage metastatic prostate cancer. Recently it has been shown that Xgeva can also delay bone metastases in CRPC patients by four months. Although no overall survival benefit was demonstrated, Xgeva will likely gain approval to expand the label in 2012, broadening its addressable population in prostate cancer. We did not include Xgeva in figures 2 or 3 as the RANK Ligand inhibitor is not considered a direct anti-tumor agent.

First-line chemotherapy: Taxotere (docetaxel). In May 2004, the FDA approved Taxotere based on two Phase III studies comparing Taxotere with mitoxantrone in patients with advanced prostate cancer, which showed a 2.9-month OS benefit (HR=0.79). In both studies, TAX-327 and SWOG 99-16, Taxotere produced a statistically significant OS benefit over mitoxantrone.

Post-Taxotere therapy: Zytiga (abiraterone). Johnson & Johnson’s Zytiga gained approval in the United States in April 2011 for mCRPC patients who progressed after Taxotere treatment. Interim analysis of the Phase III study reported a 3.9-month benefit in OS (14.8 months versus 10.9 months) with a hazard ratio of 0.65, the lowest hazard ratio achieved in large prostate cancer studies to date. Final analysis demonstrated a survival benefit of 4.6 months (15.8 months versus 11.2 months). Johnson & Johnson gained Zytiga through the acquisition of Cougar Biotechnology in July 2009 for roughly \$1 billion.

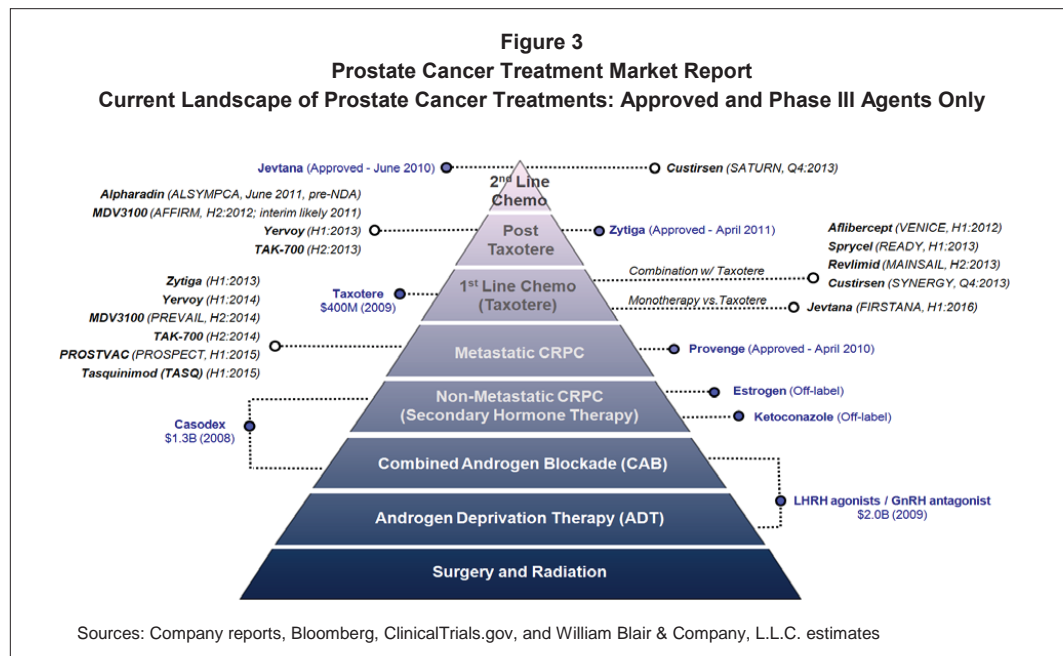
Second-line chemotherapy: Jevtana (cabazitaxel). The “second-generation” taxane, Jevtana, gained regulatory approval as a second-line treatment of mCRPC in Taxotere failures after results from the Phase III TROPIC study showed an increase in median OS of 2.4 months for Jevtana versus mitoxantrone (HR=0.70). There were also 5% treatment-related deaths in the study, as a result of the drug’s toxicity. Although both were approved in the same Taxotere-failure setting, we believe Zytiga will be used ahead of Jevtana because of its better efficacy and more favorable safety profile.

Castration-Resistant Prostate Cancer (CRPC)

As discussed above, when the cancer continues to proliferate despite castrate level of androgens, the disease has reached the CRPC stage. And unfortunately, when the CRPC progresses to the metastatic stage, the disease has transitioned to be lethal, with median survival time ranging from 12 to 24 months. We focus this section on the metastatic CRPC (mCRPC) stage, for which many agents are in clinical development. We review the competitive landscape below, focusing on Phase III agents only.

Competitive Landscape of mCRPC by Treatment Stages

Four concentrated areas for clinical development. As illustrated in figure 3, there are four areas of concentrated clinical activities: frontline mCRPC (pre-Taxotere), in combination with Taxotere, post-Taxotere second-line therapies, and second-line chemotherapy. We illustrate the Phase III agents and our estimates of the timing of their Phase III data releases in figure 3.



Frontline mCRPC: Provenge is approved and recommended as front-line therapy; at least six agents are in Phase III; Zytiga is used off-label in this setting. Before Provenge's approval, Taxotere was the recommended front-line therapy. The benchmark in this setting was Taxotere's 2.9-month overall survival benefit (HR=0.79) and its poor safety and tolerability profile typical of a chemotherapy. Dendreon is aiming to establish Provenge in the market—as the first-ever approved immunotherapy—as standard of care for mCRPC before moving to chemotherapy. Provenge offers a 4.1-month OS benefit (HR=0.759), with an excellent safety and tolerability profile as compared with Taxotere.

Other agents in Phase III studies in this setting include Zytiga (abiraterone, Johnson & Johnson), MDV3100 (Medivation and partner Astellas), Yervoy (ipilimumab, Bristol-Myers Squibb), TAK-700 (orteronel, Takeda), and tasquinimod (Active Biotech and partner Ipsen). Zibotentan (AstraZeneca) failed an interim analysis in September 2010. We also include Prostavac (Bavarian Nordic) in figure 3; a single pivotal Phase III study PROSPECT will be initiated during fourth quarter 2011.

We note that since Zytiga's approval in the post-Taxotere setting in April 2011, it has been used off-label in the front-line mCRPC setting as well. We discuss this practice in detail in later sections.

First-line chemotherapy, Taxotere: four agents in combination with Taxotere, and one agent head-to-head against Taxotere, in Phase III. In this setting, four agents are in Phase III studies in combination with Taxotere against a Taxotere-alone arm, each with a distinct mechanism of action: aflibercept (Regeneron and partner Sanofi), Sprycel (dasatinib, Bristol-Myers Squibb), Revlimid (lenalidomide, Celgene), and custirsen (OncoGenex and partner Teva). Zibotentan (AstraZeneca) failed in this setting in August 2011.

In addition, Sanofi recently initiated a Phase III study of Jevtana versus Taxotere in this setting, trying to push Jevtana to the first-line chemotherapy setting from its current second-line setting.

Post-Taxotere: Zytiga approved in this setting in April 2011; three agents in Phase III and one agent at pre-NDA stage. Zytiga (abiraterone) is now established as the best care in this setting after its approval in April 2011, posting a 4.6-month benefit in OS (15.8 months versus 11.2 months, HR=0.65) in its Phase III study in mCRPC patients who failed Taxotere. Multiple agents are in Phase III studies in this setting, including MDV3100, Yervoy, and TAK-700. Sutent (Pfizer) failed an interim analysis in September 2010 in this setting.

Further, in June 2011, alpharadin (Algeta and partner Bayer) was reported to have significantly improved OS in mCRPC patients with multiple skeletal metastases and significant bone pain (14.0 months versus 11.2 months, HR=0.699) in the Phase III ALSYMPCA Study. Alpharadin is a bone-seeking radionuclide of alpha-emitter radium-223 (²²³Ra); after intravenous administration, alpharadin travels to the lesions in the bone and kills cancer cells via radiation, which reaches 2 to 8 cells in distance. This study provides direct proof that targeting bone metastases in prostate cancer can prolong survival. Alpharadin is at the pre-NDA stage and could be approved during first half 2012.

Second-line chemotherapy, Jevtana; one agent in Phase III, and another one entering Phase III before year-end 2011. Jevtana was approved in June 2010 in the post-Taxotere setting based on a 2.4-month OS benefit (15.1 months versus 12.7 months, HR=0.70), with an unappealing safety profile that included 5% toxic deaths. Now with the approval of Zytiga in the same setting, we believe Zytiga will be used ahead of Jevtana because of better efficacy and safety profiles. After patients fail Zytiga, they may be offered Jevtana.

Custirsen (OncoGenex and partner Teva) is in Phase III in combination with Taxotere re-treatment or Jevtana in patients who failed Taxotere, with a pain palliation endpoint. Cabozantinib (Exelixis) will enter Phase III later in 2011 in patients who failed Taxotere or Jevtana with a composite endpoint of pain relief and bone scan response. We did not include cabozantinib in figure 3, as the detailed design of the Phase III study is not yet known.

Competitive Landscape of mCRPC by Mechanisms of Action

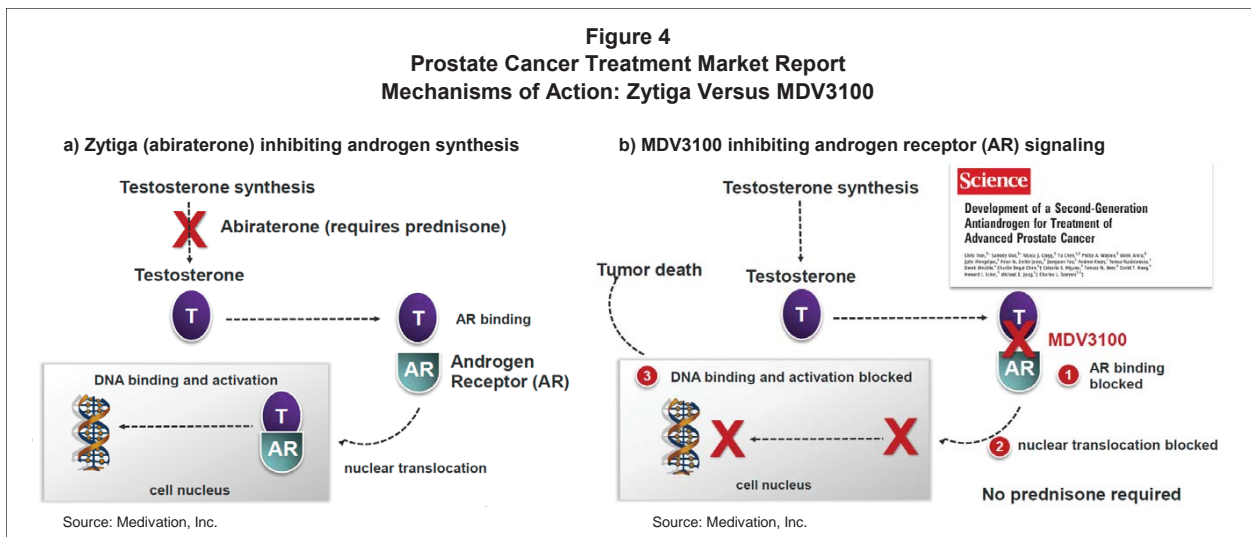
AR signaling plays the key role in the continuum of the prostate cancer disease; current hormonal agents are suboptimal. Prostate cancer is an androgen (mostly testosterone) dependent disease, and activation of the androgen pathway is the key mechanism for prostate cancer growth at all stages of the disease. There are two ways of blocking the AR signaling pathway: blocking androgen synthesis, and/or blocking the AR activities.

LHRH agonists such as Lupron (leuprolide acetate) and Zoladex (goserelin acetate) down-regulate the synthesis of androgens, while anti-androgens such as Casodex (bicalutamide) target the ARs by preventing androgens from binding to ARs. The two mechanisms are sometimes combined as the disease progresses to achieve a more complete blockage of AR signaling.

The current hormonal agents are suboptimal due to two major reasons: 1) the testis is not the sole source of androgens; low levels of androgens are synthesized from the adrenal and intra-tumoral sources, which the current agents do not block; and 2) ARs could be mutated or amplified and thereby continue signaling in the presence of very low levels of androgen.

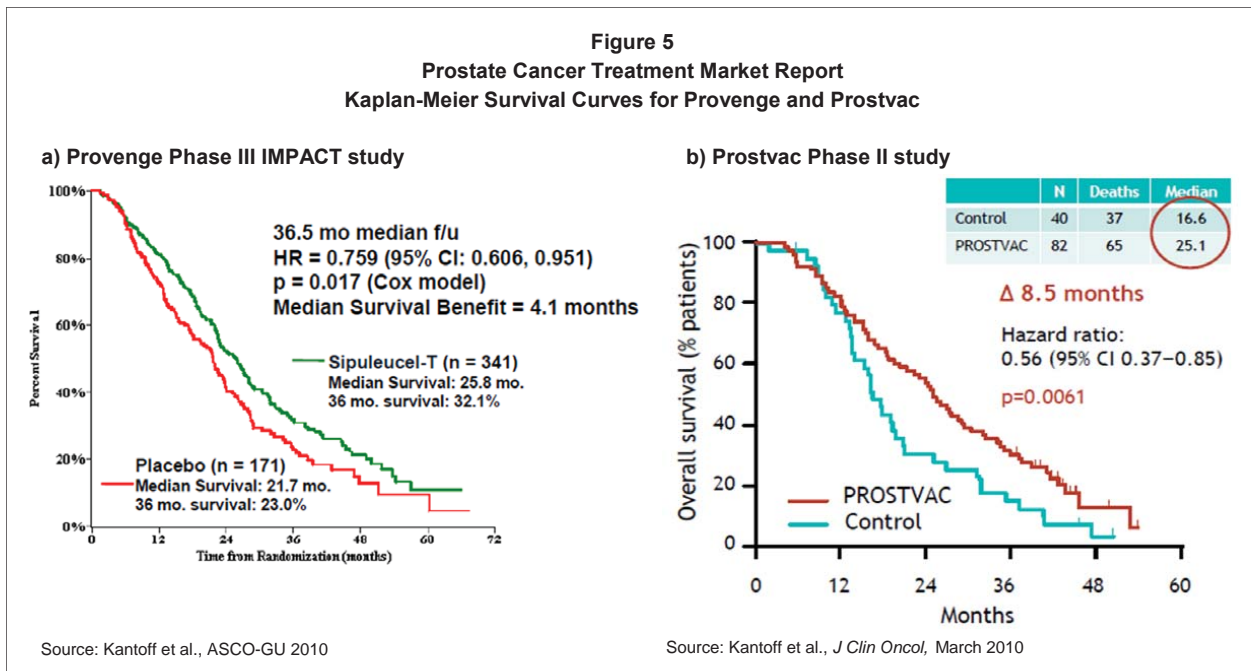
New hormonal agents:

- *Abiraterone is an improved blocker of androgen biosynthesis (figure 4a).* Abiraterone is a selective and high affinity inhibitor of CYP17A, a key enzyme in the androgen biosynthesis pathway in both the testes and the adrenal glands. We noted earlier and in figure 2 that ketoconazole is used off-label in prostate cancer, as it is a nonspecific inhibitor of CYP17A and exhibited anti-tumor activity. However, ketoconazole has significant dose-limiting toxicities including fatigue, neurotoxicity, hepatotoxicity, and nausea. Abiraterone has exhibited about 10-fold higher activity than ketoconazole, with a better safety profile. We note that the composition of matter and use patents of abiraterone are set to expire in 2014 and Johnson & Johnson will likely obtain a five-year extension under the Hatch-Waxman Act; meanwhile, manufacturing process patents could go as far as 2025.
- *MDV3100 is a next-generation anti-androgen that achieves more complete blockage of the AR pathway (figure 4b).* The androgen receptor is a member of the steroid-receptor family. When in the unbound state, the AR is an unstable protein located in the cytoplasm of the cell. When androgen binding occurs, the complex is translocated into the nucleus, recruits co-activators, and binds to the DNA, resulting in activation of downstream targets. MDV3100 blocks the AR activation process at three distinct steps: competitively binding to AR, inhibiting translocation to the nucleus, and preventing DNA binding inside the nucleus (figure 4b). As compared with the most used anti-androgen, Casodex (\$1.3 billion in sales in 2008), MDV3100 has 8 times higher affinity to the AR, can overcome AR mutations resistant to Casodex, and appears to be a true AR antagonist—Casodex has partial AR agonism, resulting in weakened efficacy.
- *TAK-700.* TAK-700 is similar to abiraterone in mechanism of action and is in Phase III studies in both the pre-Taxotere and post-Taxotere settings, with almost exactly the same design, as illustrated in figure 3. TAK-700 is also in a Phase II study in combination with Taxotere. The whole TAK-700 program is two to three years behind Zytiga (abiraterone).



Immunotherapy:

- *Therapeutic vaccines: Provenge leads the way; Prostavac to enter Phase III during fourth quarter 2011.* Provenge was approved in the United States for asymptomatic or minimally symptomatic mCRPC in April 2010, with an OS benefit of 4.1 months and an HR of 0.759 (figure 5a). We note that Provenge is an individualized, cell-based therapeutic vaccine; the patient's cells are taken outside the body via leukopheresis, cultured with stimulating fusion peptides (PAP-GM-CSF) in vitro, and infused back into the body to elicit immune response against the prostate cancer cells. Prostavac, developed by Bavarian Nordic, an off-the-shelf vaccine, will enter a pivotal Phase III study during fourth quarter 2011, with potential entry into the market in 2015. Prostavac demonstrated an impressive 8.5-month OS benefit with an HR of 0.56 in a randomized Phase II study previously (figure 5b).



- *Immune modulators: Yervoy (ipilimumab) and Revlimid (lenalidomide).* Yervoy is an anti-CTLA antibody developed by Bristol-Myers Squibb that has recently been approved in melanoma. It is a “check point” antibody designed to break immune tolerance. It is

in Phase III studies in both the pre-Taxotere and post-Taxotere settings in mCRPC as a single agent, and earlier stage studies of the antibody in combination with other therapeutic vaccines (such as GVAX, Cell Genesys and now BioSante) are ongoing. Major side effects associated with Yervoy include immunologic reactions, particularly in the gastrointestinal system and the skin. Revlimid, produced by Celgene, is an immune modulator approved for multiple myeloma. It is in a Phase III study in mCRPC in combination with Taxotere.

Other mechanisms:

- *Blocking the VEGF pathway.* We note that Avastin, an antibody against VEGF, failed a Phase III study in prostate cancer; and Sutent, a small molecule targeting the VEGF receptor and a few other tyrosine kinases, failed the interim analysis of its Phase III study in September 2010. Regeneron and partner Sanofi are testing aflibercept, their VEGF-trap candidate, in combination with Taxotere. Tasquinimod (TASQ), from Active Biotech and partner Ipsen, works to block new blood vessels from forming. It is in a Phase III study in the pre-Taxotere setting.
- *Endothelin A receptor antagonist.* As discussed above, zibotentan failed the Phase III studies in the frontline mCRPC setting, as well as the setting of combination with Taxotere.
- *Bcr-Abl inhibitor.* Sprycel (dasatinib) is approved for CML, and is in a Phase III study in mCRPC, in combination with Taxotere.
- *Target cell survival mechanism employing anti-sense.* Custirsen is an anti-sense candidate against clusterin, which is overexpressed when cells are under stress, such as in chemotherapy. It is in a Phase III study (SYNERGY) in combination with Taxotere, and a second Phase III study (SATURN) in the post-Taxotere setting in combination with Taxotere or Jevtana. We note that while SYNERGY has OS as the primary endpoint, SATURN's primary endpoint is pain relief.

We summarize marketed and Phase III agents by mechanism of action in table 1.

Exciting New Agents That Will Change the Treatment Paradigms

Provenge, Abiraterone, and MDV3100 Should Have Strong Impact on the Treatment of Prostate Cancer; Custirsen Also Appears Promising in Combination

We believe Provenge, an immunotherapy, and the next-generation hormonal agents Zytiga (abiraterone) and MDV3100 will bring dramatic changes and advancement to the prostate cancer treatment field in the next decade.

We believe Provenge, together with other immunotherapy approaches, is likely to educate, change, and reshape the treatment paradigm in the market. Provenge's commercial performance relative to its profile and its positioning in the competitive landscape will be closely watched and eventually become a case study for immunotherapies as a therapeutic class.

Abiraterone and MDV3100 both target the well-validated AR pathway, thus they have a higher chance of success than agents of other, more novel mechanisms, in our opinion. We believe these two agents will move earlier into the hormone-sensitive stages of the disease, although they are currently approved or studied in the mCRPC settings. Between the two agents, we believe MDV3100 will likely move forward furthest along the disease continuum, followed by abiraterone, based on MDV3100's more favorable safety profile and potentially better efficacy.

Custirsen is an anti-sense therapy targeting the cell survival protein clusterin, which is over-expressed when cancer cells experience stress, such as from chemotherapy. Based on such mechanism, custirsen is being studied in combination with Taxotere and Jevtana in mCRPC

Table 1
Prostate Cancer Treatment Market Report
Competitive Landscape of Approved and Phase III Agents for Prostate Cancer Treatment by Mechanisms of Action

Drug	Brand Name	Class	Company	Treatment Stage		
				Before Docetaxel	With Docetaxel	After Docetaxel
Leuprolide†	Lupron/Eligard	LHRH agonist	Takeda/Abbott/Sanofi/Astellas	Marketed	--	--
Goserelin	Zoladex		AstraZeneca/Kissei	Marketed	--	--
Triptorelin	Trelstar		Ipsen/Watson	Marketed	--	--
Histrelin	Vantas		Endo/Teva	Marketed	--	--
Degarelix	Firmagon	GnRH antagonist	Ferring	Marketed	--	--
Bicalutamide†	Casodex	Anti-androgen	AstraZeneca	Marketed	--	--
Flutamide†	Eulexin		Merck/Teva	Marketed	--	--
MDV3100	--		Medivation/Astellas	Phase III	--	Phase III
Ketoconazole	--	CYP17A inhibitor (nonspecific)	--	Off-label		
Abiraterone	Zytiga	CYP17A inhibitor	Johnson & Johnson	Phase III	--	Approved April 2011
TAK-700	Orteronel	C17, 20 lyase inhibitor	Takeda	Phase III	--	Phase III
Docetaxel	Taxotere	Chemo: Taxane	Sanofi		Marketed	
Cabazitaxel	Jevtana	Chemo: Taxane	Sanofi	--	--	Approved June 2010
Mitoxantrone†	Novantrone	Chemo: Type II topoisomerase Inhibitor	EMD Serono/Astellas**	--	--	Marketed
Sipuleucel-T	Provenge	Immunotherapy: autologous cellular	Dendreon	Approved April 2010	--	--
Ipilimumab	Yervoy	Immunotherapy: anti-CTLA-4 antibody	Bristol-Myers Squibb	Phase III	--	Phase III
Lenalidomide	Revlimid	Immunotherapy: immunomodulator	Celgene	--	Phase III	--
ProstVac-VF/Tricom	PROSTVAC	Immunotherapy: off-the-shelf vaccine	Bavarian Nordic	Phase III §	--	--
Alpharadin	--	Alpha-pharmaceutical (radium-223 chloride)	Bayer/Algeta	--	--	Positive June 2011
Tasquinimod	--	Anti-angiogenesis	Active Biotech/Ipsen	Phase III	--	--
Zibotentan	--	Endothelin A receptor antagonist	AstraZeneca	<i>Phase III failed</i>	<i>Phase III failed</i>	--
Dasatinib	Sprycel	Bcr-Abl inhibitor	Bristol-Myers Squibb	--	Phase III	--
Aflibercept	ZALTRAP	Anti-angiogenesis	Regeneron/Sanofi	--	Phase III	--
Custirsen	--	Clusterin antisense oligonucleotide	OncoGenex/Teva	--	Phase III	Phase III

‡ Estimated sales for prostate cancer only

† Generic version available

** Acquired rights following acquisition of OSI Pharmaceuticals (2010)

§ Initiation expected in mid-2011

Sources: Company reports, Bloomberg, ClinicalTrials.gov, and William Blair & Company, L.L.C.

patients, with top-line data due in fourth quarter 2013. Among the agents that are in Phase III development in combination with Taxotere as illustrated in figure 3, custirsen is the only one that has demonstrated a large OS benefit in a randomized, placebo-controlled Phase II study (23.8 months versus 16.9 months, HR=0.61), and also significant pain palliation. Should it be approved, custirsen could offer not only survival but also pain benefits to the key chemotherapy agents in prostate cancer. Further, custirsen's mechanism of action supports its use with chemotherapies in other cancer indications as well; in fact, OncoGenex and Teva are in the process of initiating a Phase III study in non-small cell lung cancer (NSCLC) as well.

In a League of Its Own: Provenge Is the First Immunotherapy Ever Approved

Therapeutic vaccines for cancer are an old and elegant concept, but the development pathways have been lined with many failures, including Canvaxin (from CancerVax), Oncophage (Antigenics), GVAX (Cell Genesys, now being revived by BioSante), PanVac (Therion), and Stimuvax (in breast cancer, developed by Merck KGa). The definitive demonstration of an OS benefit for Provenge is a milestone and has led to renewed excitement for the field of cancer immunotherapy.

Difficulties in immunotherapy: many lessons learned. After years of trial and error, it is evident now that for an immunotherapy to work, multiple components are necessary to optimize its effects: the right antigens that are cancer-specific, the right delivery system, the right adjuvants; all these have to not only be recognized by the immune system, but also potent enough to elicit immune responses that will attack tumors, and such attacks must result in prolonged overall survival (OS). Further, it is also crucial to study the right population that is most likely to respond (earlier disease stages make more sense than terminal disease for immunotherapy), catch the disease at the right stage (neoadjuvant versus metastatic stages), be patient enough to detect delayed response (for example, the OS Kaplan-Meier curves for Provenge and placebo separated at eight months), and pick the right endpoint (overall survival, not progression-free survival, as evidenced by Provenge and Prosvac studies).

Table 2
Prostate Cancer Treatment Market Report
Summary of Provenge Phase III Data

	D9901		D9902A		IMPACT (D9902B)	
	Sipuleucel-T N=82	Placebo N=45	Sipuleucel-T N=65	Placebo N=33	Sipuleucel-T N=341	Placebo N=171
Median Overall Survival (OS), months	25.9	21.4	19.0	15.7	25.8	21.7
Hazard Ratio (HR)	0.586		0.787		0.759	
p-value	0.010 †		0.331 †		0.017 ‡	
Median Survival Benefit, months	4.5		3.3		4.1	
Survival rate (36-month), %	34.1%	10.7%	31.6%	21.2%	31.7%	23.0%
Median Time to Progression (TTP), weeks	11.7	10.0	10.9	9.9	14.6 **	14.4 **
95% Confidence Interval, weeks	9.1 - 16.6	8.7 - 13.1	9.3 - 17.7	8.4 - 18.0		
Hazard Ratio (HR)	0.69		0.92		0.95	
p-value	0.052 †		0.719 †		0.628 †	

† log rank test; ‡ Cox model

** Referred to as time-to-objective-disease progression (ODP)

Sources: Small et al., *JCO* 2006;24:3089-94; Kantoff et al., *ASCO-GU* 2010; Higano et al., *Cancer* 2009;115(16):3670-9; and William Blair & Company, L.L.C.

Provenge approval and label. As summarized in table 2, Provenge was approved after three Phase III studies for mCRPC that is asymptomatic or minimally symptomatic. Provenge extended OS versus placebo in a statistically significant fashion in two of the Phase III studies, D9901 and IMPACT. D9902A was discontinued early. However,

pooled data of D9901 and D9902A showed an OS benefit of 4.3 months (23.2 months versus 18.9 months) and hazard ratio of 0.67, similar to IMPACT (Higano et al., *Cancer* 2009; 115:3670-9).

No apparent benefit in progression-free survival (PFS) despite definitive OS benefit: maybe a “class effect” of immunotherapy. Although the OS benefit was clear, there was no PFS (PSA progression, tumor progression, or bone metastases) benefit from Provenge treatment. Interestingly, Prostavac also demonstrated no PFS benefit but a profound OS benefit (8.5 months, HR=0.55) in its Phase IIb study. It is hypothesized that vaccines may induce delayed responses not seen in the first few months, but the immune responses generated ultimately slow tumor growth.

Such “class effect” of no PFS but significant OS benefit is proving hard for the cancer community to accept in the early stage of commercial launch of Provenge. More meaningful measurement catered to immunotherapy may be needed to better define the benefit of immunotherapy, and biomarkers to track induction and magnitude of immune response and/or clinical benefit will be helpful too in increasing commercial acceptance.

Delayed effect on Kaplan-Meier curve: another “class effect” of immunotherapy. We note that most chemotherapies demonstrate a separation on the OS Kaplan-Meier curves from the very beginning; in contrast, immunotherapies exhibit delayed separation on the KM curves (see figure 5, on page 9, for Kaplan-Meier curves for both Provenge and Prostavac).

In general, it makes tremendous sense for immunotherapy to be administered early. Dendreon aims to move Provenge into the hormone-sensitive stage, but it may take a while to get there. In our opinion, immunotherapy is an elegant concept and if it works, the earlier the disease stage, the more benefit it may elicit and the more cost effective the therapy will be. Dendreon is expected to initiate a large study of Provenge in hormone-sensitive prostate cancer in 2013, which could increase its treatable population from the current 40,000 in mCRPC setting to 100,000-200,000 in the United States. The challenge is that using OS as the endpoint in the hormone-sensitive setting will require a very long study, and at present, there are no other convincing endpoints to definitively demonstrate clinical benefit. We note that Study P11 (a Phase II study) of Provenge in hormone-sensitive disease demonstrated encouraging trends in time to biochemical failure (PSA increase), PSA-DT (PSA-doubling time), and time to distant metastases. However, additional larger studies are needed to demonstrate definitively the benefits in a statistically significant fashion, and agreement on approvable endpoints has to be reached with the FDA for any potential label extensions.

Impact on current practice. With Provenge's launch into the market, both oncologists and urologists are being educated to more aggressively identify patients that fit Provenge's on-label indication: an mCRPC disease state with minimal burden, especially those who are still asymptomatic. Theoretically, administering Provenge early will likely lead to better outcomes, thus maximizing the cost effectiveness of the therapy. Still, such a hypothesis needs to be definitively proved by clinical studies.

Despite its academic significance, Provenge commercial uptake has proved to be slow. It has been over a year since the commercial launch of Provenge, the first approved immunotherapy ever to show a definitive OS benefit. As of the quarter ending June 30, 2011, Provenge cumulative sales were \$126 million, with an annual run-rate of \$200 million exiting the quarter. This represents about 1,355 patients treated since launch, given the \$93,000 price tag per treatment. We note that the eligible mCRPC patients for Provenge are estimated at over 40,000 in the United States. The launch trajectory was initially constrained by manufacturing capacity; however, it still tracked significantly below management's internal projections and the Street consensus. In August 2011, during the second-quarter earnings call, management withdrew its previous 2011 sales guidance of \$350 million-\$400 million, leading to the substantial fall of the stock price.

Cost, reimbursement, skepticism on efficacy, cumbersome administration, slow patient identification, and competition limit uptake. The “buy and bill” model for Provenge has created financial inconvenience, as physicians have to pay for the cost of Provenge out of pocket first and get reimbursed later, a lag that lasted months; we note that the \$93,000 full price is incurred within a month. The National Coverage Decision (NCD) and the Q code issuance in July 2011 should expedite the reimbursement process and the concern on reimbursement might be eased in the coming months.

Further, we find that the community is still battling to accept the intractability of benefit from Provenge, as no signs of slower disease progression are expected from Provenge administration (for example, no PSA decline), and there are no biomarkers or assays to track the performance of the therapy. In addition, it takes time to educate urologists and oncologists to proactively identify Provenge candidate patients who are metastatic but not yet symptomatic, and doctors, especially the urologists, need to get comfortable infusing in the offices too, as the Provenge production and administration process, as described in detail in later sections, is not trivial.

Most importantly, competition from Zytiga off-label use in the front-line mCRPC setting is starting to affect Provenge uptake, and we believe in the long term, Zytiga, MDV3100, and Prostavac will depress Provenge sales. We discuss the impact of such competition in detail below.

Abiraterone Versus MDV3100

Mechanism of action: both target the AR pathway, with MDV3100 acting downstream of abiraterone. As discussed earlier and shown in figure 4, abiraterone acts to block synthesis of androgens, while MDV3100 works at the AR level to block the signaling pathway.

Certain in vitro evidence suggests that MDV3100 might be more effective in salvaging abiraterone failures than the other way around, because MDV3100 acts downstream of abiraterone and may be a more complete blocker of the AR signaling pathway. It will be interesting to see the performance of MDV3100 and abiraterone in crossover studies as they attempt to rescue each other’s failures.

Similar clinical programs: MDV3100 is 15 months behind abiraterone. As summarized in table 3, the Phase III programs of abiraterone and MDV3100 are similar in design, with MDV3100 trailing abiraterone by about 15 months.

Both agents’ first Phase III programs are in the post-Taxotere setting (COU-AA-301 and AFFIRM), and the second Phase III programs in chemo-naive, frontline mCRPC patients (COU-AA-302 and PREVAIL). Because of the shared mechanism with ketoconazole, in abiraterone studies, patients with prior ketoconazole exposure were excluded. We note that a prior study demonstrated that abiraterone is more effective in ketoconazole-naive patients than experienced patients.

Abiraterone achieves unprecedented HR of 0.65 in the Phase III study in the post-Taxotere setting (COU-AA-301). As discussed previously, interim analysis of the Phase III study of abiraterone in the post-Taxotere setting in September 2010 demonstrated statistically significant PFS (5.6 versus 3.6 months, HR=0.67) and OS (14.8 months versus 10.9 months, HR=0.65) benefit. The HR of 0.65 in OS is the best in any large prostate cancer studies to date. The study was stopped based on the positive interim analysis and all eligible patients were crossed over to abiraterone. Subsequently, Zytiga (abiraterone) was approved within four months of NDA submission, in April 2011.

We believe the abiraterone success bodes well for MDV3100’s AFFIRM interim analysis by year end 2011 in the post-Taxotere setting. MDV3100 acts downstream of abiraterone in the AR pathway, and the Phase I/II data in the post-Taxotere setting looked comparable between the two agents (summarized in table 6, on page 19). As a result, we believe the success of abiraterone bodes well for the AFFIRM study, where MDV3100 is studied in the post-Taxotere setting as well.

Table 3
Prostate Cancer Treatment Market Report
Phase III Programs of MDV3100 and Zytiga (abiraterone)

	Patient Population	Number; Randomization	Dosage; Schedule	Primary Endpoint(s)	Secondary Endpoint(s)	Study Start Date	Complete Enrollment	Phase III Readout (Est.)
MDV3100								
AFFIRM	mCRPC patients; post-Taxotere	1199 2:1 - MDV3100:placebo	160 mg QD	Overall Survival	Progression-free survival, safety & tolerability	September 2009	November 2010	Interim readout YE:2011; Final H2:2012
PREVAIL	mCRPC patients; chemo-naïve	1680 1:1 - MDV3100:placebo	160 mg QD	Overall Survival, Progression-free survival	Time to first skeletal-related event, Time to initiation of cytotoxic chemotherapy	September 2010	Q1:2012	H2:2014
Zytiga (abiraterone)								
COU-AA-301	mCRPC patients; post-Taxotere; ketoconazole naïve	1158 2:1 - Abiraterone:placebo	1000 mg QD + prednisone, 5 mg BID	Overall Survival	Proportion of patients achieving a PSA decline \geq 50%	May 2008	July 2009	Interim readout: September 2010
COU-AA-302	mCRPC patients; chemo-naïve ketoconazole-naïve	1000 1:1 - Abiraterone:placebo	1000 mg QD + prednisone, 5 mg BID	Overall Survival, Progression-free survival	--	May 2009	May 2010	H1:2013

Sources: Company reports, ClinicalTrials.gov, and William Blair & Company, L.L.C estimates

In the pre-Taxotere or frontline mCRPC setting, MDV3100 might demonstrate more striking data than abiraterone in Phase III studies. While the data is comparable in the post-chemo setting between the two agents, in the pre-chemo setting, MDV3100 has demonstrated much better time-to-PSA progression (TTPP) as compared with abiraterone (60 weeks versus 32 weeks). In patients who were ketoconazole-naïve, TTPP was 116 weeks for MDV3100 and 71 weeks for abiraterone. Time to radiologic progression also appeared impressive at 56 weeks; although the corresponding data for abiraterone in its Phase I/II study has not been reported, we note that in Provenge pivotal studies, the TTP was about 14.5 weeks (summarized in table 4, on page 17).

Abiraterone is in a pivotal study, COU-AA-302, in this setting, with data expected late 2012 or early 2013, and MDV3100's PREVAIL study with a similar design is about 15 months behind. We believe it is likely that MDV3100 will eventually produce better PFS and OS data in this setting than abiraterone.

MDV3100 appears to have a more favorable safety profile than abiraterone, and does not need prednisone co-administration. Adverse events most commonly seen with the abiraterone+prednisone regimen include fluid retention (30.5% versus 22.3%), hypokalemia (17.1% versus 8.4%), hypertension (9.7% versus 7.9%), liver function test abnormalities (10.4% versus 8.1%) and cardiac disorders (13.3% versus 10.4%), as compared to prednisone alone.

For MDV3100, the most common adverse event is fatigue. In addition, in the previous Phase I/II study, there were two witnessed cases of seizures that occurred at high MDV3100 doses of 600 mg QD and 360 mg QD, and one possible seizure at 480 mg QD. It is unclear whether MDV3100 was responsible for the seizures, as both patients who had witnessed seizures were taking concurrent medications that could contribute to a lower seizure threshold, and had other medical conditions that could have contributed to the seizures (hypocalcaemia needing

IV calcium, anemia needing red-cell transfusions, and skull metastases needing skull radiation). We note that MDV3100 is dosed at 160 mg QD in all Phase III studies, a dose that is substantially lower than the doses where seizures were seen. We also note that no seizures were observed previously at 160 mg QD, and fatigue was seen as no different from placebo at this dose. Although a lower dose, 160 mg QD is considered to be sufficient for maximum AR binding; higher doses would not further increase the inhibitive effect of MDV3100 (Scher et al., *Lancet* 2010; 375:1437-46). Finally, the AFFIRM study has completed enrollment of 1,199 patients and PREVAIL is enrolling; to date, the Data and Safety Monitoring Board has been allowing the studies to continue, suggesting a satisfactory safety profile thus far.

Prednisone is co-administered with abiraterone to lower the incidence and severity of hypertension, hypokalemia, and fluid retention. We note that long-term administration of prednisone is associated with immunosuppressive effects, especially when the dose exceeds 10 mg daily for two months or more. In contrast, MDV3100 is an oral monotherapy that does not require prednisone.

Both agents can move earlier along the disease continuum into hormone-sensitive prostate cancer, but MDV3100 could move further into earlier disease than abiraterone because of its better safety profile, in our opinion. We note that abiraterone can be viewed as an improved ketoconazole and it may eventually move to the hormone-sensitive stage of the disease, and MDV3100 could also move earlier in the treatment sequence to replace Casodex to capture a bigger market share. The Phase II TERRAIN study of MDV3100 against Casodex is testing this hypothesis. Taking it one step further, Medivation and Astellas recently initiated another Phase II study to examine MDV3100 in hormone-naive patients, as a frontline hormonal treatment to replace LHRH agonists.

Given MDV3100's better safety profile and no need for prednisone, as discussed above, we believe MDV3100 could eventually move into earlier disease stages than abiraterone.

It is easier to combine or sequence MDV3100 with Provenge or other immunotherapy. As MDV3100 does not require prednisone co-administration, it can be combined with immunotherapy or sequenced either before or after. Further, MDV3100 is hypothesized to promote T cell maturation, and thus will likely potentiate the effect of the immunotherapy as well.

In General, Overall Survival for Future Studies Will Be Confounded

With the availability of Provenge, Taxotere, Jevtana, and Zytiga, the OS results for the ongoing Phase III studies in both the frontline mCRPC setting and the post-Taxotere setting will likely be confounded. After a patient progresses in a clinical trial, either on the active arm or the placebo arm, he may elect to receive any of the available therapies in no particular sequence. If the options and the sequence of the options are not balanced well between the active arm and the placebo arm, the OS data will likely be confounded and/or compromised; the interpretation will likely be complicated. This will pose a general problem to all the Phase III studies in progress, including for MDV3100, TAK-700, tasquinimod, and Prostavac. We note, however, that the PFS data will not be compromised, as the patients usually are not allowed to receive another therapy before they progress in the clinical study.

CTC is being studied as a potential predictive marker for OS in prostate cancer. Previous smaller studies have shown that the number of circulating tumor cells (CTC) is a more predictive marker than PSA for OS in prostate cancer. CTC is now being studied prospectively in all Phase III studies for abiraterone, MDV3100 and others. Data in the next few years may elucidate its utility. A good predictive marker for OS would at least partly solve the issue of confounding OS as described above, and could inform studies in earlier stage of the disease where the OS is usually much longer than that in the later disease setting.

At a Glance: Summary of Data

The tables on the following pages provide a summary of data from approved agents and those in Phase III trials for use in frontline, in combination with Taxotere, and post-Taxotere mCRPC settings.

Study Data	mCRPC First-Line Treatments									
	Docetaxel + prednisone	Mitoxantrone + prednisone	Sipuleucel-T	Placebo	Abiraterone	MDV3100	TAK-700	Tasquinimod	PROSTVAC	Placebo
	N=335	N=337	N=341	N=171	N=42 (5% prior keto)	N=65	N=97	N=134	N=82	N=40
	Phase III (TAX-327)		Phase III (IMPACT)		Phase II (COU-AA-001)	Phase III (S-3100-1-01)	Phase II (TAK-700-201)	Phase II (07TAS008)	Phase II (TBC-PRO-002)	
Dosing Schedule	75 mg/m ² , q3 weeks/ 5 mg/day, BID	12 mg/m ² , q3 weeks/ 5 mg/day, BID	3 doses, q2 weeks	3 doses, q2 weeks	250 - 2000 mg, QD (Dose ranging study)	20 - 600 mg, QD (Dose ranging study)	300 - 600 mg, QD (Dose ranging study)	0.25 - 1 mg, QD (Dose escalating study)	7 sub-q doses, days 1 -140	7 sub-q doses, days 1 -140
Patient population	Metastatic hormone-refractory prostate cancer		Asymptomatic or minimally symptomatic mCRPC					Aymptomatic mCRPC	Minimally symptomatic mCRPC	
Efficacy										
Overall Survival (OS), median	19.2 months	16.3 months	25.8 months	21.7 months	--	--	--	--	25.1 months	16.6 months
Hazard Ratio	0.79 (0.67, 0.93)	--	0.759 (0.606, 0.951)	--	--	--	--	--	0.56 (0.37, 0.85)	--
p-value	0.004	--	0.017 *	--	--	--	--	--	0.0061 **	--
Progression-free survival (PFS), median	--	--	--	--	--	--	--	7.6 months vs 3.3 months	--	--
Hazard Ratio	--	--	--	--	--	--	--	0.57	--	--
p-value	--	--	--	--	--	--	--	0.0009	--	--
Time-to-Progression (TTP), median	--	--	14.6 weeks	14.4 weeks	--	56 weeks	--	--	3.8 months	3.7 months
Hazard Ratio	--	--	0.95 (0.77, 1.17)	--	--	--	--	--	0.88 (0.57, 1.38)	--
p-value	--	--	0.628 **	--	--	--	--	--	0.6 **	--
Response Rate (by RECIST or PCWG2)										
Complete	--	--	--	--	--	--	--	--	--	--
Complete / Partial	12%	7%	--	--	38% (9/24)	36% (9/25)	12% (6/49)	6% (4/134)	--	--
Stable Disease	--	--	--	--	28% (7/24)	44% (11/25)	51% (25/49)	55% (36/134)	--	--
Overall	--	--	--	--	--	--	--	--	--	--
Decrease in serum PSA, percentage										
30% or greater	--	--	--	--	71%	71%	--	--	--	--
50% or greater	45%	32%	--	--	67%	62%	53%	--	--	--
90% or greater	--	--	--	--	19%	--	25%	--	--	--
Decline in CTC Count, percentage										
Conversion from 5 or greater to less than 5	--	--	--	--	59% (10/17)	75% (12/16)	--	--	--	--
Decline by 50% or greater	--	--	--	--	--	--	--	--	--	--
Decline by 30% or greater	--	--	--	--	70% (12/17)	--	--	--	--	--
Time to PSA Progression (TTPP), median	~ 33 weeks	~ 34 weeks	--	--	~ 32 weeks	60 weeks	--	--	--	--
					71 weeks in keto naive	116 weeks in keto naive	--	--	--	--
Survival rate, 36-month, %	18.6%	13.5%	32.1%	23.0%	--	--	--	--	--	--
Adverse Events (Grade 3/4)			All Trials ◊		All Grades	All 140 subjects †			All Grades	
Hematological										
Neutropenia	32%	22%	--	--	--	--	--	--	--	--
Febrile neutropenia	3%	2%	--	--	--	--	--	--	--	--
Leukopenia	--	--	--	--	--	--	--	--	--	--
Thrombocytopenia	1%	1%	--	--	--	--	--	--	--	--
Anemia	5%	2%	2%	2%	--	3%	--	3%	--	--
Increase lipase or amylase	--	--	--	--	--	--	--	6%	--	--
Non-Hematological										
Diarrhea	2%	1%	0%	1%	--	--	3%	--	9%	15%
Nausea	3%	2%	1%	0%	--	--	2%	1%	21%	5%
Fatigue	5%	5%	1%	1%	--	11%	11%	--	43%	20%
Asthenia	--	--	1%	1%	--	2%	--	--	--	--
Back pain	--	--	3%	3%	--	--	--	--	--	--
Hypertension	--	--	--	--	40%	--	--	--	--	--
Hypokalaemia	--	--	--	--	88% ‡	--	6% ¶	--	--	--
Anorexia	1%	< 1%	0%	1%	--	3%	1%	--	--	--
Seizure	--	--	--	--	--	2%	--	--	--	--
Sepsis (non-neutropenic)	--	--	--	--	--	2%	--	--	--	--
Stomatitis	--	--	--	--	--	--	--	--	--	--
Chills	--	--	2% §	0%	--	--	--	--	15%	3%
Arthralgia	1%	1%	2%	2%	12%	--	--	--	12%	25%
Dyspnea	3%	1%	2%	1%	--	--	--	--	--	--
Hematuria	--	--	1%	1%	--	--	--	--	--	--
Pyrexia	--	--	1% §§	1%	--	--	--	--	18%	15%
Headache	--	--	1%	0%	10%	--	--	--	--	--
Vomiting	--	--	--	--	--	--	--	--	--	--
Myalgia	--	--	--	--	--	--	--	--	--	--
Peripheral oedema	--	--	--	--	--	--	--	--	--	--
Nasal congestion	--	--	--	--	--	--	--	--	--	--
Constipation	--	--	0%	1%	--	--	--	1%	11%	15%
Fluid retention	1%	< 1%	--	--	31%	--	--	--	--	--
Renal failure	--	--	--	--	--	--	--	4%	--	--
Deep vein thrombosis	--	--	--	--	--	--	--	4%	--	--
Cardiac failure	--	--	--	--	--	--	--	1%	--	--
Dizziness	--	--	--	--	--	--	--	--	12%	8%
Erythema	--	--	--	--	--	--	--	--	59%	55%
Pain	--	--	--	--	--	--	--	5%	35%	35%
Swelling	--	--	--	--	--	--	--	--	28%	13%
Pruritus	--	--	--	--	--	--	--	--	21%	10%
Induration	--	--	--	--	--	--	--	--	12%	15%
Peripheral oedema	--	--	--	--	--	--	--	--	13%	10%

◊ AEs: Grade 3 - 5, Pooled results from all randomized, controlled trials
 * Cox Model adjusted for PSA and LDH
 ** Hazard ratio based on unadjusted Cox Model (not pre-specified), p-value based on a log-rank test (not pre-specified)
 † log-rank test
 § Chills: All Grades - 53.1% vs. 10.9% for Sipuleucel-T and placebo, respectively
 §§ Fever: All Grades - 31.3% vs. 9.6% for Sipuleucel-T and placebo, respectively
 ‡ Managed by epinephrine or glucocorticoid replacement
 † Adverse events reported for all 140 subjects of S-3100-1-01 trial, both chemo-naïve and chemo-refractory
 ¶ Any grade Hypokalemia, 10%

Sources: Company reports and William Blair & Company, L.L.C.

Table 5
Prostate Cancer Treatment Market Report
Summary of Data of Phase III Agents in Combination with Taxotere (docetaxel)

	Phase II: OGX-011-03		Phase I: AAAB3212	Phase III: CA180086
	Custirsen (OGX-011)		Revlimid (lenalidomide)	Sprycel (dasatinib)
	+ Docetaxel	Docetaxel	+ Docetaxel	+ Docetaxel
	(650 mg Q1W + 75 mg/m ² Q3W)	(75 mg/m ² Q3W)	(10 mg QD + 60 mg/m ² Q3W) §	(50 mg QD + 60 mg/m ² Q3W) §§
	N=41	N=41	N=34	N=46
Baseline Patient Characteristics				
Age (years), median	69	69	70	65
Prior chemotherapy	0%	0%	41%	30%
ECOG performance status				
0	51%	49%	--	57%
1	49%	51%	--	39%
Measurable disease, n (%)				
No	34%	41%	38%	33%
Yes	66%	59%	62%	67%
Bone/nodal metastases only				
Yes	66%	59%	--	--
No	32%	41%	--	--
PSA, ng/ml				
≤ 100	49%	49%	--	--
> 100	51%	51%	--	--
Median	110	110	102	--
Gleason score				
≤ 7	34%	44%	--	--
8-9	68%	54%	--	--
Progression at random assignment				
Objective	12%	22%	--	--
PSA	85%	78%	--	10%
Median predicted 24-month survival rate, %	25.6%	19.6%	--	--
Baseline serum clusterin, µg/ml (range)	46 (15 to 158)	53 (16 to 156)	--	--
Efficacy				
Median number of cycles, n	9	7	8	--
Patients receiving any subsequent therapy, n (%)	28 (70%)	22 (54%)	--	--
Investigational agent	10 (25%)	11 (27%)	--	--
Anti-androgen therapy	23 (58%)	22 (54%)	--	--
Median treatment duration	--	--	--	4.8 months
Median duration of response	--	--	9.4 months	--
PSA decline				
PSA decline of ≥ 50%, n (%)	23 (58%)	22 (54%)	15 (44%)	21 (49%)
PSA decline of ≥ 30%, percent	65%	59%	--	--
Measurable disease response (evaluable patients)	N=26	N=22	N=23	N=31
Complete response (CR), n (%)	0	0	1 (4%)	0
Partial response (PR), n (%)	5 (19%)	6 (25%)	5 (22%)	13 (42%)
Partial response, unconfirmed (uPR), n (%)	--	--	--	3 (10%)
Stable disease (SD), n (%)	20 (77%)	12 (50%)	11 (48%)	5 (16%) [†]
No change, n (%)	--	--	9 (29%)	9 (29%)
Progressive disease (PD), n (%)	1 (4%)	4 (17%)	6 (26%)	1 (3%)
Progression-free survival (PFS), median	7.3 months	6.1 months	--	--
Hazard ratio (HR)	0.88	--	--	--
PSA progression-free survival, median	8.8 months	8.5 months	--	--
Time-to-progression (TTP), median	--	--	6.6 months	--
Overall survival (OS), median	23.8 months	16.9 months	--	--
Hazard ratio (HR)	0.61	--	--	--
p-value	0.06	--	--	--
Median change in serum clusterin, percent				
Cycle 1 - Day 15	- 13 *	+ 2	--	--
Cycle 1 - Day 22	- 26 **	+ 1	--	--
Time of confirmed PSA decline of ≥ 50%	- 17	0	--	--
Time of PSA progression	- 9	- 10	--	--
Decrease in uNTx levels ≥35%, percent	--	--	--	50%
Decrease in BAP levels from baseline, percent	--	--	--	75%
Reduction in size and/or no. of bone lesions, percent	--	--	--	28%
Safety				
Discontinuations				
Due to adverse events (AEs) ^{††} , percent	30%	12%	--	--
Due to disease progression, percent	18%	39%	--	--
Common adverse event (AEs), grades 3-4	N=40	N=41	--	N=46
Hypersensitivity	--	--	--	2%
Low hemoglobin	0%	7%	--	--
Anemia	--	--	--	2%
Leukopenia	45%	54%	--	--
Neutropenia	73%	63%	26%	--
Lymphopenia	53%	22%	--	--
Fatigue	10%	22%	--	4%
Neuropathy (sensory)	5%	7%	--	--
Rigor/chills	10%	2%	--	--
Nausea	3%	10%	--	--
Febrile neutropenia	10%	12%	--	--
Dehydration	0%	7%	--	--
Thrombosis	8%	5%	--	--
Pleural effusion	--	--	--	2%
Fever (grades 1-2)	45%	12%	--	--
Elevated creatinine (grades 1-2)	20%	5%	--	--

§ Dose escalated to 40 mg QD and 75 mg/m², respectively

§§ Dose escalated to 120 mg QD and 75 mg/m², respectively

† Stable disease ≥ 18 weeks

†† Due to AEs or refusal of further treatment

uNTx: Urinary N-telopeptide

* p-value = 0.05; ** p-value = 0.005

Sources: Company reports, *Journal of Clinical Oncology* (Vol. 28, No. 27, September 2010, pp 4247-4254); ASCO 2009 Abstract Numbers 5061 and 5156; BioCentury; and William Blair & Company, L.L.C.

Table 6
Prostate Cancer Treatment Market Report
Summary of Data of Approved and Phase III Agents in the Post-Taxotere Setting in mCRPC

	Post-Taxotere Treatments					Comments
	Cabazitaxel + prednisone N=378	Mitoxantrone + prednisone N=377	Abiraterone + prednisone N=1195 (prior keto excluded)	Placebo + prednisone N=58 (47% prior keto)	Abiraterone + prednisone N=58 (47% prior keto)	
Study Data		Phase III (TROPIC)	Phase III (COU-AA-301)	Phase I/II (COU-AA-004)	Phase I/II (S-3100-1-01)	
Dosing Schedule	25 mg/m2, q3 weeks/ 5 mg/day, BID	12 mg/m2, q3 weeks/ 5 mg/day, BID	1000 mg, QD / 5 mg/day, BID	-- / 5 mg/day, BID	1000 mg, QD / 5 mg/day, BID	20 - 600 mg, QD (Dose ranging study)
Efficacy						
Overall Survival (OS), Median	15.1 months	12.7 months	15.8 months	11.2 months	--	--
Hazard Ratio	0.70 (0.59, 0.83)		0.65 (0.54, 0.77)			
p-value	< 0.0001		< 0.0001			
Progression-Free Survival (PFS), Median	2.8 months	1.4 months	5.6 months †	3.6 months †	--	5.8 months (175 days)
Hazard Ratio	0.74 (0.64, 0.86)		0.67 (0.58, 0.78)			
p-value	< 0.0001		< 0.0001			
Time to PSA Progression (TTPP), Median	6.4 months	3.1 months	10.2 months	6.6 months	(169 days)	5.5 months (166 days)
Hazard Ratio	0.75 (0.63, 0.90)		0.58 (0.46, 0.73)			--
p-value	0.001		< 0.0001			--
Response Rate (by RECIST or PCWG2)						
Complete/Partial Stable Disease	9.2%	7.7%	--	--	18% (4/22)	12% (4/34)
Decrease in Serum PSA, Percentage					59% (13/22)	53% (18/34)
30% or greater	--	--	--	--	--	62%
50% or Greater	39%	18%	38% **	10%	36% at wk 12	51% at wk 12
90% or greater	--	--	--	--	--	--
Decline in CTC Count, Percentage						
Conversion From 5 or Greater to Less Than 5	--	--	--	--	34%	37% (13/35)
Adverse Events (Grade 3/4)						
Hematological ††						All 140 subjects §
Neutropenia	82%	58%	--	--	--	--
Febrile neutropenia	7%	1%	--	--	--	--
Leukopenia	69%	42%	--	--	--	--
Thrombocytopenia	4%	2%	--	--	--	--
Anemia	11%	5%	--	--	--	3%
Nonhematological						
Diarrhea	6%	< 1%	--	--	--	--
Nausea	2%	< 1%	--	--	--	--
Fatigue	5%	3%	--	--	--	11%
Asthenia	5%	2%	--	--	--	2%
Back pain	4%	3%	--	--	--	--
Fluid retention	--	--	2.3%	1.0%	--	--
Hypokalaemia	--	--	3.8%	0.8%	--	--
Hypertension	< 1%	< 1%	1.3%	0.3%	--	--
Liver function test abnormalities	--	--	3.5%	3.0%	--	--
Cardiac disorders	--	--	4.1%	2.3%	--	--
Arthralgia	--	--	--	--	--	2%
Seizure	--	--	--	--	--	2%
Hematuria	2%	1%	--	--	--	--
Vomiting	2%	0%	--	--	--	--
Dyspnea	1%	< 1%	--	--	--	--
Arrhythmia	1%	< 1%	--	--	--	--

‡ 5 mg/day, BID (either prednisone or prednisolone)

† Radiographic Progression-Free survival (rPFS)

†† Based on laboratory values, cabazitaxel: N=369, mitoxantrone: N=370

§ Adverse events reported for all 140 subjects of S-3100-1-01 study - both chemo-naïve and chemo-refractory

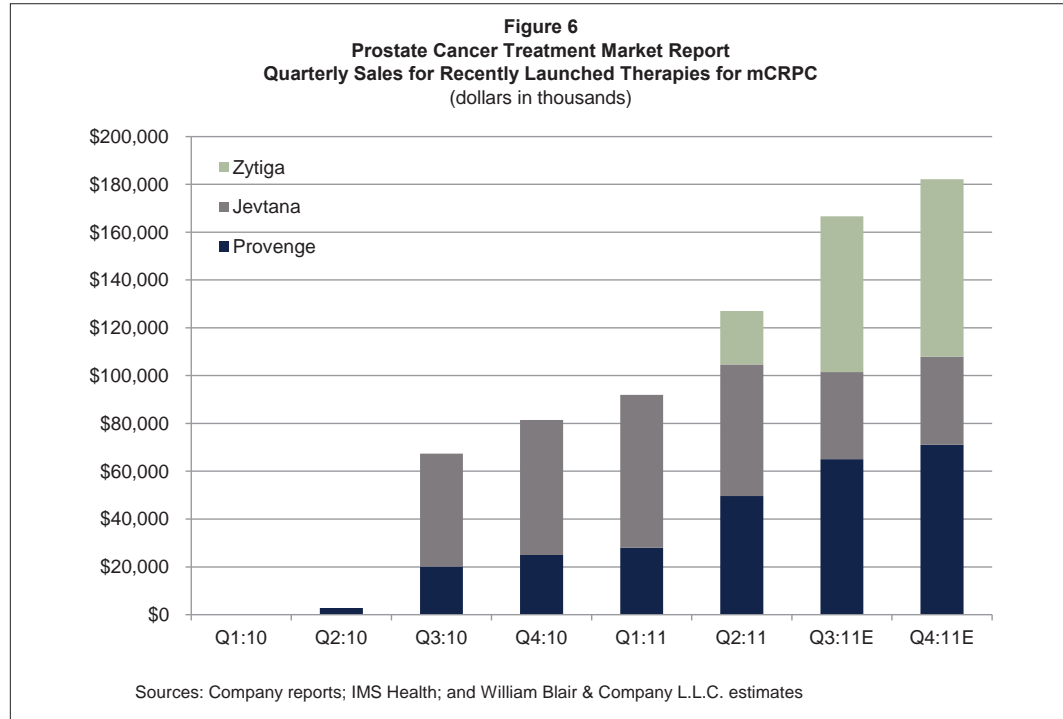
** Total PSA response - p<0.0001

Sources: Company reports and William Blair & Company, L.L.C.

What Might the Future Landscape for Prostate Cancer Look Like?

2011-2012: Zytiga (Abiraterone) Established as Standard of Care in Post-Taxotere Setting, and Used Off-Label in the Pre-Taxotere, Frontline mCRPC Setting

We summarize the sales performance of the three new agents approved during the past one and half years in figure 6.



Provenge sales have been increasing quarter-over-quarter since its approval in April 2010, with a noticeable jump from first quarter 2011 to second quarter 2011, as a result of additional capacity in the New Jersey facility coming online, partly easing the capacity constraints. Now with all three facilities fully functional and with capacity constraint no longer an issue, the demand appears to be losing steam.

Jevtana started strong after its approval in June 2010, but we forecast that use of Zytiga will depress its sales, as Zytiga will be sequenced in front of Jevtana in patients who failed Taxotere and lead to a “delay-to-peak” effect for Jevtana. It is clear from figure 6 that for third quarter 2011 to date, Zytiga has eaten into Jevtana’s sales significantly.

Priced at \$5,000 per month, the average price per course of Zytiga is \$40,000 given the average treatment duration of eight months in the approved post-Taxotere setting. Jevtana is priced at \$8,000 per 3-week cycle and an average treatment course lasts 6 cycles, resulting in total cost of \$48,000. In contrast, Provenge is priced at \$93,000.

In addition, the NCCN (National Comprehensive Cancer Network) recommends Zytiga (abiraterone acetate) not only in the approved setting of post-Taxotere, but also in the pre-Taxotere setting together with Provenge (NCCN Guidelines: Prostate Cancer, Version 4.2011), ahead of the readout of the Phase III study (COU-AA-302). It is difficult to assess how much off-label use is manifested in the sales numbers, but we believe the off-label use of Zytiga will only go up in the future. Such trend will overtake shares from Provenge in this setting and keep pressure on its sales growth.

The dilemma of sequencing Provenge and abiraterone. As noted previously, abiraterone needs prednisone co-administration. As long-term administration of glucocorticoids is associated with immunosuppressive effects, especially when the dose of the glucocorticoid exceeds the equivalent of about 10 mg of prednisone daily for two months or more, it may not be optimal to administer abiraterone immediately after a patient progresses on Provenge as the immunosuppressive effect of prednisone may weaken the therapeutic effect of Provenge. As a result, empirically Provenge should be given at least six months prior to abiraterone, according to some experts. Similarly, it is probably not rational to combine Provenge and abiraterone either. A practical sequence may be to give abiraterone first, and after patients progress, Provenge could be prescribed after a washout period.

We are not aware of any studies ongoing at this time to inform the community how to properly use Provenge in the face of competing agents.

Provenge followed by Taxotere may be a synergistic sequence of therapies. We note that an earlier study demonstrated promising response to Taxotere after Provenge (Petrylak et al., *Chemotherapy Symposium* 2006). For the 51 patients with mCRPC treated with Provenge and then followed by Taxotere, the OS was 34.5 months, versus 25.4 months for the 31 patients who received placebo first and then Taxotere ($p=0.023$). It is hypothesized that chemotherapy after the immunotherapy may alter the tumor cells and trigger a “danger signal” that leads to cell death, thereby capitalizing on an ongoing immune response.

This hypothesis of whether chemotherapy will be beneficial after a vaccine is being tested in a Phase II study of Prostavac conducted by the Eastern Cooperative Oncology Group. Patients with mCRPC will be randomized to one of two arms: Taxotere, or Prostavac followed by Taxotere. The primary endpoint is OS.

We note that in this sequence, Taxotere is also co-administered with prednisone at 5 mg twice daily. The weakening effect on immune response from the steroid may be offset by the strong anti-tumor effect from Taxotere.

2012-2013: Zytiga Frontline mCRPC Data Release, Beating Provenge for the Same Label
As stated previously and summarized in table 6, abiraterone achieved a 4.6-month OS benefit and an HR of 0.65 in the post-Taxotere setting. Based on such data, we believe abiraterone will likely achieve a higher OS benefit in the frontline chemo-naive setting, the setting that Provenge is approved for. Provenge’s 4.1-month OS benefit and HR of 0.759 in this setting could be beaten by abiraterone in 2013 when the data is released. In addition, abiraterone could also demonstrate significant PFS benefit in this setting, which Provenge failed to demonstrate.

2011-2014: Provenge Struggles Commercially in the Face of Strong Abiraterone Competition

As an oral drug that is less expensive and with better PFS and OS data (due in 2013), abiraterone could further depress Provenge’s market share, in our opinion, if no clear information is available to the academic and physician community about what incremental benefit Provenge could provide to patients.

2014: MDV3100 Data in Frontline mCRPC Could Beat Abiraterone

As discussed earlier, while in the post-Taxotere setting the data between MDV3100 and abiraterone were comparable, the Phase I/II data in the frontline mCRPC setting for MDV3100 appeared to be better than abiraterone, likely because MDV3100 more completely blocks the AR pathway than abiraterone, and the mCRPC frontline setting is more AR-dependent than the post-Taxotere setting.

We believe MDV3100 will produce better PFS and likely OS data than abiraterone in this setting as the Phase III PREVAIL study reads out in 2014.

2015: Prostavac Could Be a Truly Successful Immunotherapy for Prostate Cancer

Better HR in OS, although in a small Phase II study. Prostavac is a vaccine consisting of the tumor antigen PSA and co-stimulatory molecules to help boost immune response. It is an off-the-shelf vaccine that does not require individualized therapy, and therefore will not have demand constraints or supply logistic challenges as Provenge. The vaccine involves seven subcutaneous injections over a three-month period. The Phase II study conducted from November 2003 to July 2005 demonstrated an 8.5-month OS benefit (25.1 months versus 16.6 months, $p=0.0061$, $HR=0.56$; see figure 5), seemingly better than Provenge achieved in IMPACT. It is interesting to note that for both studies, the median OS for the active arms was remarkably similar at around 25 months; however, the placebo was much worse in the Prostavac study as compared with IMPACT. If Prostavac demonstrates a comparable OS benefit as Provenge in its Phase III study, data from which is expected in 2014-2015, physicians and patients may prefer Prostavac over Provenge based on such data.

Off-the-shelf vaccine offers advantages in manufacturing, distribution, and COGS. Prostavac is an off-the-shelf vaccine that is easy to manufacture and distribute, compared with Provenge's high logistical demand being an autologous cellular vaccine. Prostavac also has lower COGS, and could compete on pricing when necessary.

Various Phase II studies are in progress to support potential broader Prostavac use. As the Phase III study is under way, a number of Phase II studies are being conducted to understand Prostavac's potential use in other settings; such data will aid in label expansion and compendia listing efforts once Prostavac is approved for the first setting.

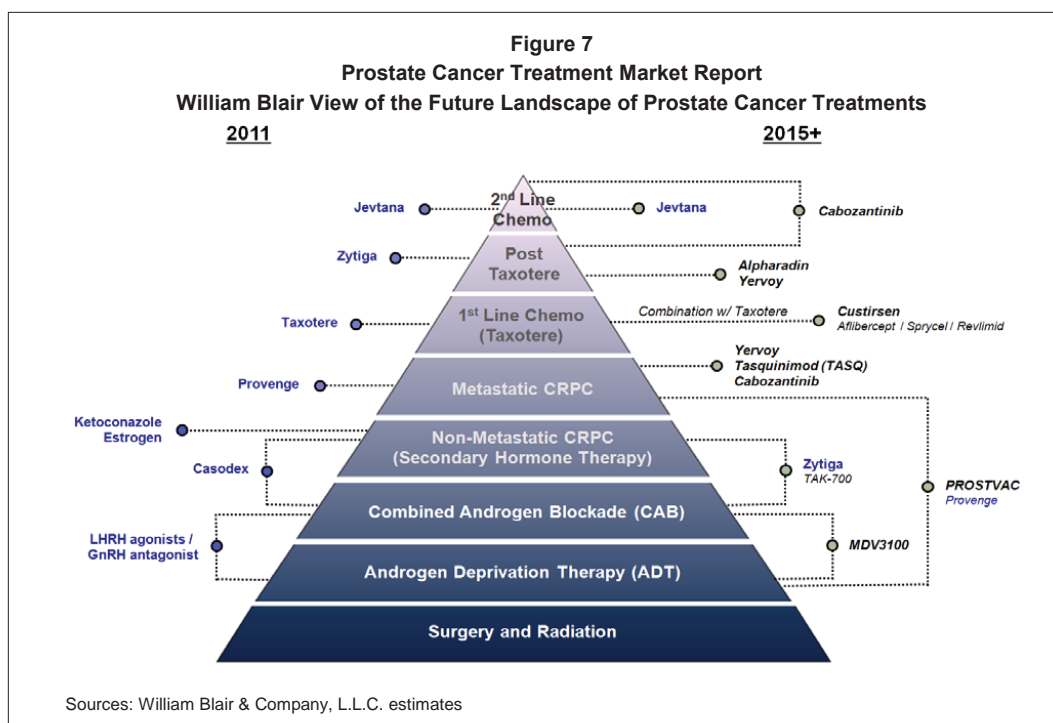
Current Phase II studies include 1) Taxotere treatment preceded with Prostavac or placebo in mCRPC patients, as described earlier, with an OS endpoint; 2) in combination with flutamide, an anti-androgen, in nonmetastatic patients, with a time-to-progression endpoint; 3) in combination with samarium, a radioactive drug, in mCRPC, with a PFS endpoint; 4) frontline therapy ahead of hormonal agents after local therapy, with PSA progression as endpoint; 5) in combination with Yervoy in mCRPC patients, with a PSA response endpoint; and 6) intraprostatic injection in progressive or locally recurrent prostate cancer, with a PSA response endpoint. Fortunately for Bavarian Nordic, all six Phase II studies are funded by the National Cancer Institute, totaling 378 patients. These studies cover the full spectrum of the prostate cancer disease continuum.

In contrast, very few studies of Provenge are ongoing in settings other than the on-label setting. This could be due to financial constraint, and its cumbersome production, administration and supply process.

2013-2014: Custirsen Might Be Established as the Companion for Chemotherapies Should the SYNERGY and SATURN studies be positive around year-end 2013, custirsen could be established as the combination of choice with chemotherapies, both Taxotere and Jevtana, to enhance OS and provide pain palliation.

Beyond 2015: Our Thoughts on the Future Treatment Paradigm of Prostate Cancer We illustrate our thoughts on the present and future prostate cancer treatment paradigms in figure 7.

2011. At present, after local therapy, hormonal agents such as LHRH agonists and Casodex are used to inhibit the AR pathway. If the disease progresses, secondary hormonal treatments such as ketoconazole and estrogen are used to further stifle the AR pathway. Once the disease progresses to the metastatic stage, Provenge is the frontline therapy, although Zytiga is also used in this setting off-label at the present time. Once patients progress after Provenge treatment, they are subject to Taxotere, the first-line chemotherapy. Failing Taxotere, patients would go on to Zytiga, followed by second-line chemotherapy Jevtana, if they are fit enough.



2015 and beyond. As illustrated in figure 7, we envision the suboptimal hormonal agents used today will be replaced by more effective hormonal agents in 2015 and beyond. We believe MDV3100 could be used following local therapy. Zytiga could be used after MDV3100 or as an add-on to MDV3100 for a combined androgen blockade. The use of these two agents in early stage prostate cancer might significantly prolong the time to progression and enhance survival.

In parallel to the medical castration approach, immunotherapy could flourish as well. If Prostavac can demonstrate significant OS benefit in 2014-2015 from its pivotal Phase III study in the frontline mCRPC setting, and multiple Phase II studies that are in progress in earlier disease settings also demonstrate benefit in delay of disease progression at that time, Prostavac could be used in front of, or in combination with, the novel hormonal agents such as MDV3100, in our opinion. Provenge could move here as well, but it might be more challenging because of its cumbersome production and administration, and also the fact that few Phase II studies are being conducted in earlier settings with Provenge now.

After failing MDV3100, Zytiga, and/or Prostavac, patients progress to the mCRPC stage. At this point, the disease state will be very different from the mCRPC we are seeing today; it will be much more advanced, as it has failed much better hormonal agents. Whether Provenge could continue to be effective in these patients and catch these patients as a frontline mCRPC therapy will likely be questionable.

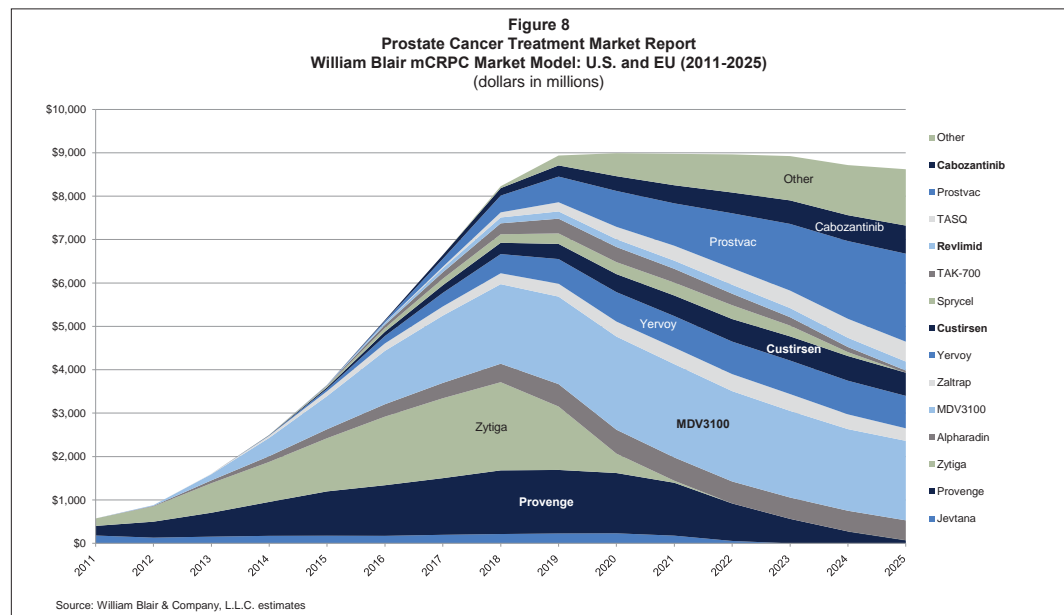
At this stage of disease, other biological pathways might overtake the AR pathway to be the main drivers to promote tumor growth. Pathways involving angiogenesis, c-Met, cell survival, TGF-beta, and integrin, among others, are known to be activated when the AR pathway is inhibited. We envision agents such as Yervoy, tasquinimod, and cabozantinib to play roles in this setting, providing alternative mechanisms of action to treat the disease with a very different biology.

Chemotherapy will likely remain an important option for prostate cancer. In combination with Taxotere will be custirsen or other agents such as aflibercept, Sprycel, and Revlimid. After Taxotere, alparadin, Yervoy, Jevtana, and cabozantinib could be used as the next options. Alparadin specifically target bone metastases, and cabozantinib will be beneficial in clearing bone metastases and provide pain relief as well.

William Blair Market Model for Prostate Cancer Therapies

Figure 8 illustrates our view of the prostate cancer treatment market in the next 15 years. The relative market shares from different companies and their marketed or Phase III drug candidates are based on clinical data available to date, which dictates the product profile and their relative positioning and strength in the marketplace.

We acknowledge that forecasting the market in the next 15 years based on clinical data available to date might be overly ambitious and flawed and as a result inaccurate; however, such efforts illustrate well our thought process on the big picture. We expect to update this graph periodically as the medicine evolves and M&A/partnership deals are struck in the space.



Doubling of the Branded Market in the Next Decade

Before the LHRH agonists and Casodex went generic, the branded prostate cancer market worldwide was about \$4 billion. As illustrated in figure 8, we believe the new agents and a full pipeline for prostate cancer could double the market to close to \$9 billion in the next decade.

Provenge Versus Prostavac

We model Provenge capturing a peak 25% of the U.S. mCRPC market, reaching a peak of \$1.13 billion. The ramp up in the next few years will likely be depressed by competition from Zytiga, MDV3100, and others. The sustainability of its revenues in the out-years depends on the success or failure of Prostavac in 2015, in our opinion. Should Prostavac produce comparable data in the same setting that Provenge is approved in, Prostavac will likely be the major force depressing the tail of the Provenge revenue curve.

Zytiga and TAK-700

We model Zytiga going generic in 2019. Zytiga's composition-of-matter and use patents expire in 2014, and with a five-year Hatch-Waxman extension, we model brand pricing for Zytiga until 2019. Generic abiraterone will lead to slower growth of the prostate cancer treatment market

in dollar value, and will likely render TAK-700 uncompetitive in the marketplace, as TAK-700 is not well differentiated from abiraterone, in our view. Should the manufacturing patents of abiraterone hold up and extend protection to 2025, our market model will change accordingly.

MDV3100: A Long-Term Winner

We believe MDV3100, based on its profile as discussed previously, will move to the front-line of the disease and become a long-term winner. It will not likely be affected by generic abiraterone based on our arguments on positioning, as discussed previously.

As MDV3100 moves earlier along the disease continuum, pricing will likely come down. In the post-Taxotere setting, Zytiga prices at \$5,000 per month, and we expect MDV3100 to price at a similar level in this setting in 2012 if AFFIRM is positive. Such pricing will not be sustainable in the hormone-sensitive stage, but with a much larger addressable population and much longer treatment duration, the decrease in pricing will be more than made up, in our opinion, resulting in higher franchise value for MDV3100.

Custirsen: A Chemotherapy Companion

If custirsen establishes itself as a chemotherapy companion, it will have a steady although relatively small position in the marketplace, as illustrated in figure 8.

Cabozantinib: A Unique Contribution

Among the Phase III or near-Phase III agents, cabozantinib stands out because of its striking profile in anti-tumor activity and ability to clear bone metastases and provide pain relief. Phase III programs for the VEGFR-2 and c-Met dual inhibitor are still in planning, but we envision a position in the marketplace for it.

Investment Conclusions

We Are Concerned About Provenge's Commercial Prospect

Negatives

Uncertainty on uptake in the United States. Our conversations with thought leaders indicate that divergent views exist toward the Provenge data (OS benefit only) and the treatment modality (general skepticism toward immunotherapy), and the headwinds in educating the market and pushing adoption may lead to slower uptake. Key questions being asked include how to integrate the vaccines into clinical practice, how to assess the effect of the immunotherapy, and whether there are predictive factors to indicate which populations would respond more.

Strong competition from novel oral agents competing with and moving in front of Provenge. We believe the use of oral agents such as abiraterone and MDV3100 in the same setting of Provenge will depress its near term uptake. In the future, the oral agents may migrate off-label to the hormone-sensitive stage, prolonging the time to progress to metastatic disease, and as a result, lowering the incidence each year in mCRPC. Although Provenge may eventually capture these patients at the mCRPC stage, it would take longer for it to reach the peak penetration. Further, as discussed previously, the mCRPC that fails MDV3100 and abiraterone will be very different than the mCRPC we are seeing today. It is not clear to us whether Provenge can be perceived to be effective in the more aggressive mCRPC in the future, or whether new studies need to be conducted for Provenge to keep an established position in the front-line mCRPC setting.

Competition from within the immunotherapy class. Potential competition from other vaccines such as Prostavac in three to four years could further erode Provenge market share. We discussed previously that data from the Prostavac Phase II study was very impressive

(8.5-month OS benefit, HR=0.55; see figure 5, on page 9). A single 1,200-patient Prostavac Phase III study will be initiated during fourth quarter 2011. If Prostavac demonstrates an OS benefit similar to Provenge, its ease of manufacturing and distribution as well as lower COGS will likely render it competitive against Provenge in the marketplace. We note that Prostavac is an off-the-shelf vaccine with a long shelf life, while Provenge is an autologous cellular vaccine that is patient-specific, and the process of making Provenge is more complicated and has to be finished within a strict time frame. Fixed costs, variable costs, COGS, and start-up costs are much higher for Provenge, and managing the supply chain is no easy feat either.

The EU opportunity is big, but likely muted. It is estimated that there are twice as many mCRPC patients in the European Union as in the United States; therefore, the EU represents a large opportunity for Dendreon. Dendreon plans to submit the MAA for Provenge by year-end 2011, and expect potential approval in 2013. We note the following obstacles that may mute the European opportunity:

1. High pricing may lead to limited uptake in certain EU states, especially in cost sensitive countries such as the United Kingdom.
2. Abiraterone data in the same frontline mCRPC setting will be out in 2013 and it is highly likely that the HR will be better than that of Provenge, in our opinion. With an oral therapy that has better data and is more cost effective, most EU countries may adopt abiraterone more readily than Provenge, or use abiraterone at earlier stage of the disease, leading to a delayed-to-peak effect for Provenge.
3. Certain European counties, such as Germany, the largest market in Europe, have passed legal regulations requiring companies to demonstrate incremental benefit of their therapy, and that incremental benefit will be rigorously evaluated. In the face of abiraterone, and potentially MDV3100, it might be difficult for Dendreon to provide a strong argument of incremental benefit from Provenge without supporting clinical data.
4. Prostavac data may mature in the 2014-2015 time frame as well, and this is a direct competitor to Provenge in the same immunotherapy class. Further, Prostavac is an off-the-shelf vaccine, much easier to manufacture and distribute.

As a result, we model peak penetration of 25% and 13% in the United States and the EU (60% probability of reaching the EU market in late 2013), and peak sales of \$1.13 billion and \$520 million, respectively.

Positives

High U.S. pricing. Because of the high price of Provenge (\$93,000 per patient), it does not require a high penetration rate for Provenge to reach blockbuster status and sustain a hefty valuation for Dendreon.

Strong incentive for physicians to prescribe Provenge. We note that the physicians are reimbursed for 106% of the cost of Provenge, in addition to a fee charged for infusion. Such an arrangement provides a strong incentive for physicians to prescribe Provenge. That said, we note that in the near future the reimbursement rate will likely decline to 103%, due to Medicare and Medicaid budget reforms.

We Are Bullish on MDV3100

Higher chance of success based on validated mechanism and early data. As the AR pathway is a well validated pathway that drives prostate cancer growth, MDV3100—based on its mechanism of action—is low risk, and therefore has a higher chance of success. Early data also suggested a profile of efficacy comparable to or better than abiraterone, and satisfactory safety profile at 160 mg QD.

MDV3100 has blockbuster potential. We assume worldwide sales of \$2.2 billion for MDV3100 in mCRPC, in both frontline and post-Taxotere settings. We note that Medivation and Astellas also initiated two Phase II studies in the hormone-sensitive settings, one comparing MDV3100 against Casodex, the other one in hormone naive patients; we have not included these settings in our model.

We note that the patient population could be 5 to 10 times greater at the Casodex level or at the front-line, hormone-naive level, as compared to the mCRPC level. In addition, the treatment duration will be much longer as well, months at the mCRPC level versus years at the earlier settings. As discussed previously, we believe MDV3100 pricing will come down as it moves earlier along the disease continuum, but the much larger addressable population and much longer treatment duration will more than make up for the decrease in pricing, resulting in higher franchise value for MDV3100.

We value MDV3100's mCRPC opportunity at \$35 per share. Assuming \$2.2 billion worldwide peak revenue, 75% probability of reaching the market, 50% share in the United States and 15% royalties on sales outside the United States, we derive the mCRPC opportunity at \$35 per share.

We Are Bullish on Custirsen

Custirsen is major value driver; data from two Phase III studies expected by year-end 2013. Custirsen is an anti-sense agent against the cell survival protein clusterin. It is tested in combination with chemotherapy agents to further prolong survival, provide pain relief, and improve quality of life. The SYNERGY study compares custirsen plus Taxotere with Taxotere alone in mCRPC patients, with OS as the primary endpoint. The SATURN study enrolls Taxotere failure patients and compares custirsen in combination with Taxotere or Jevtana with chemotherapy alone. We model 60% probability for success and \$570 million peak worldwide sales for custirsen and derive a price target of \$21. As a reference, we estimate that Taxotere achieved over \$400 million in sales in prostate cancer before it went generic.

Dendreon Corporation

Concerned With Provenge Commercial Prospect; Initiating Coverage With Underperform Rating and \$8 Price Target

Dendreon's Provenge is the first immunotherapy approved in the United States; as such, we believe it will eventually capture a good share of the on-label indicated market for metastatic castration-resistant prostate cancer (mCRPC) in the United States. However, we rate Dendreon Underperform, based on the following:

- Near-term market uptake of Provenge in the United States will likely remain slow, as physicians continue to weigh cost against benefit, and as community oncologists and urologists learn to adopt its use.
- Competition from off-label use of Zytiga (abiraterone) and other future agents, such as MDV3100, will depress Provenge's market share in the next few years, as these agents will likely produce better data in the same setting in which Provenge is approved and present stronger cost-benefit arguments.
- Competition from within the immunotherapy class, such as Prostavac in the 2014-2015 time frame, could further depress Provenge's market share in the out-years. As Prostavac is an off-the-shelf vaccine that is much easier to administer and distribute, we believe it will dominate the immunotherapy approaches should its Phase III data be comparable with that of Provenge.
- We are concerned about Provenge's prospects of approval and commercial potential in Europe, because of higher pricing pressure and a more-competitive environment on the continent.
- The recent withdrawal of guidance and the sharp fall in the stock price damaged management's credibility, which will take substantial time to rebuild, in our opinion.
- Our probability adjusted net present value (NPV) model suggests a 12-month target of \$8. We model a 25% peak penetration for Provenge in the United States, corresponding to \$1.13 billion peak revenue in 2017; sales would decline afterward. We assume 60% probability of reaching the market in late 2013 in Europe, achieving 13% peak penetration and peak sales of \$520 million. With a net cash of -\$3 per share at year-end 2012, we derive our price target of \$8.

Dendreon develops and markets immunotherapies that target cancers. The company's lead product, Provenge, is the first immunotherapy approved in the United States. Dendreon is based in Seattle.

Healthcare | Biotechnology

Stock Rating: **Underperform**
 Company Profile: **Aggressive Growth**
 Price Target: **\$8**

Symbol: DNDN (NASDAQ)
 Price: \$11.90 (52-Wk.: \$9-\$44)
 Market Value (mil.): \$1,771
 Fiscal Year End: December
 Dividend Yield: None

Estimates

	2010A	2011E	2012E
EPS FY	(\$3.18)	(\$2.47)	(\$1.10)
Sales (mil.)	\$48.1	\$213.8	\$368.6

Valuation

FY P/E	NM	NM	NM
--------	----	----	----

Trading Data

Shares Outstanding (mil.)	148.9
Float (mil.)	147.9
Average Daily Volume (thous.)	9,653.3

Financial Data

Total Debt/Total Capital	113%
Enterprise Value (mil.)	\$1,708
Price/Book	6.19

Investment Summary

Assessing the Potential of Provenge

We believe the key questions are how big an opportunity Provenge can be both in the United States and Europe, and how profitable the company can become given the cumbersome logistics to manufacture and distribute the patient-specific therapy.

We estimate Provenge will capture 25% of the United States and 13% of the EU mCRPC frontline market at peak and decline afterward. As illustrated in figure 8, we believe Provenge will garner some market share as a result of its novelty and benefit; however, competitors such as abiraterone and MDV3100, with their better clinical data and stronger cost-benefit arguments, will likely limit its peak uptake.

Furthermore, Prostavac, an off-the-shelf vaccine, may further depress Provenge's share beyond 2015, should Prostavac's Phase III data demonstrate results comparable with those of Provenge. Prostavac is a vaccine as well, and in a prior Phase II study it demonstrated a similar efficacy and profile as did Provenge. The major difference between the two vaccines is that Prostavac is an off-the-shelf vaccine, not an autologous vaccine like Provenge, and therefore is much easier to manufacture and distribute. Currently, there are a number of Phase II Prostavac studies in various settings, including sequencing with chemotherapy, in combination with hormonal agents, and as neoadjuvant therapy after surgery. Such Phase II data will support broad Prostavac use and its move into earlier-stage disease on the disease continuum. In contrast, there is a dearth of in-progress Phase II studies to provide data to the clinicians on how to use/sequence Provenge, and how to potentially expand the label or compendia listing down the road. This is likely due to the cumbersome production and distribution of Provenge and its prohibitive costs.

Cash flow breakeven in the United States is at \$500 million in revenue, likely achievable in 2013, with cost of goods sold at 50%. After \$200 million in start-up manufacturing costs in the United States, Provenge's cost of goods sold is currently at 58%, and projected to decline to 50% exiting 2012 and 2013, and further to 25% in the out-years. As a result, we project the company to be cash flow positive in 2013 and EPS positive in 2014. However, if revenue in the out-years declines to less than \$500 million, the franchise will have difficulty sustaining itself.

All three manufacturing facilities—New Jersey (48 workstations), Atlanta (36 workstations), and Los Angeles (36 workstations)—are in production, but operating at a low capacity, due to low demand in the upcoming months. The recent restructuring laid off 500 employees, or 25% of the company's total workforce, which will lead to better alignment of demand and staffing at the manufacturing sites.

The EU commercial prospect is uncertain, in our view. In Europe, Dendreon plans to submit the marketing authorization application (MAA) around year-end 2011, and expects potential approval in mid-to-late 2013. We believe the chance of approval in Europe is not great, and that the macroeconomic environment and the higher pricing pressure in the continent do not bode well for a therapy that is high priced with questionable tangible benefit.

By 2013, abiraterone will have been on the market for two years for the post-Taxotere setting and used off-label for the frontline mCRPC setting for which Provenge is seeking approval. In 2013 the abiraterone data in front-line mCRPC will be available and it is highly likely that the data will be better than that of Provenge. Therefore, without significant data demonstrating the potential incremental benefit of Provenge, such as when it is used in combination with other agents, it will be a hard case to argue for reimbursement in the European Union, in our opinion. Dendreon does not have active studies to answer such questions and challenges in the marketplace at the present time.

Instead of investing \$200 million-\$300 million in start-up costs to set up manufacturing, Dendreon decided to employ one or more contract manufacturing organizations in Europe to lower up-front investment. The cash flow breakeven point in the European Union will

likely be around \$400 million in revenues, and we estimate \$520 million in EU peak sales. It is not unreasonable to postulate that the NPV for the EU opportunity will be unattractive, and it may not make sense to pursue opportunities there, in our opinion.

Risks to Our Underperform Rating

Risks to our Underperform rating include better-than-expected uptake of Provenge in the U.S. market; failure of clinical studies from competitive agents such as abiraterone, MDV3100, and Prostavac; straight approval in the European Union; and commercial uptake on the continent better than our expectations.

Valuation

In building the probability-adjusted NPV model in general, we estimate the peak sales of a given drug candidate, its probability of advancing to the next stage of development and eventually reaching the market, and the company's share of revenue and expenses depending on the commercialization plan and/or structure of partnerships, if any. We then calculate the cash flows after adjusting all revenues and expenses with respective cumulative probabilities for each stage. The cash flows are then discounted back using an industry-specific weighted average cost of capital to arrive at a probability-adjusted NPV for each drug candidate. We use 10% for Dendreon, as Provenge is already an approved product. Once we determine the NPV for each candidate, we then add net cash and other costs, which include expenses not directly associated with the development of the clinical candidates, to arrive at a fair value estimate for the stock.

We estimate there are 40,000-50,000 patients annually in the United States who are diagnosed or have progressed to mCRPC with minimal or no symptoms, and such incidence grows at 4% a year. Based on rationales stated previously, we model a peak penetration rate of 25% for Provenge into these patients. With \$93,000 per patient in pricing, we estimate the Provenge peak at \$1.13 billion.

For the European Union, we assume 60% probability for Provenge to reach the market in late 2013. We model 70,000 patients eligible for Provenge in 2014 in the European Union, but peak penetration is 13% due to reasons stated earlier.

As a result, we derive valuation for Provenge in both the United States and European Union at \$11 per share. Based on estimated net cash of -\$3 per share at year-end 2012, our price target is \$8 per share.

Table 7
Dendreon Corporation
Sum-of-the-Parts Fair Value
(dollars in thousands)

Drug	Peak Sales	Stage of Development	Estimated Launch Date	Probability of Commercialization	Percentage of Sales to Company	Probability-Adjusted NPV	Value Per Share	Percentage of Fair Value
Provenge—United States	\$1,130,471	Marketed	Q2:2010	100%	100%	\$1,493,449	\$10.15	123.6%
Provenge—European Union	\$522,156	MAA Filing H1:2012	H2:2013	60%	100%	\$158,939	\$1.08	13.2%
Subtotal						\$1,652,388	\$11.24	136.7%
Net Cash at Year End 2012						(\$416,575)	(\$2.83)	(34.5%)
Net Present Value of additional Gain (Loss)*						(\$27,273)	(\$0.19)	(2.3%)
Sum-of-Parts Fair Value						\$1,208,540	\$8.22	100.0%

Sources: Company reports and William Blair & Company, L.L.C. estimates

Upcoming Catalysts

Table 8
Dendreon Corporation
Clinical Development Timeline/Milestones

Drug	Provenge (Sipuleucel-T)	DN24-02 (Neuvenge)
Indication	Castration-resistant prostate cancer	HER2/neu-positive tumors
Class	Autologous Immunotherapy	Autologous immunotherapy
Partner		
1Q 2010	Update results from Phase III IMPACT study 4.1-month survival benefit (HR=0.759, p=0.017)	
2Q 2010	FDA approval—asymptomatic or minimally symptomatic mCRPC (April 29); U.S. launch	
3Q 2010		
4Q 2010	MEDCAC meeting (November 17); Submitted sBLA for New Jersey manufacturing facility	
1Q 2011	Announce EU strategy; New Jersey facility fully one line (March); CMS—guideline publication (March 30)	
2Q 2011	FDA approval of Atlanta facility; CMS—National Coverage Assessment (June 30)	
3Q 2011	FDA approval of Orange County facility; Restructuring plan (September)	Initiate Phase II study in HER2+ urothelial carcinoma (N=180)
4Q 2011		
1Q 2012	MAA filing; Announce CMO for Europe	
2Q 2012		
3Q 2012		
4Q 2012		
1Q 2013	Initiate M1 study (Provenge+ADT vs. ADT alone, N=1680, mADPC)	
2Q 2013	EU approval and launch	
3Q 2013		
4Q 2013		

Brown highlight: Events likely to affect the stock price
mADPC: metastatic androgen-dependent prostate cancer

Sources: Company reports and William Blair & Company, L.L.C. estimates

Management Team

We list key management team members of Dendreon in table 9.

Management	Position	Previous Experience
Mitchell H. Gold, M.D.	President and Chief Executive Officer	Vice President and Chief Business Officer, Dendreon Corporation; Vice President, Data Critical Corporation; Chief Executive Officer and President, Co-founder, Elixix Corporation; Physician, Department of Urology at the University of Washington. Dr. Gold received his B.S. from the University of Wisconsin-Madison and his M.D. from Rush Medical College in Chicago.
Mark W. Frohlich, M.D.	Executive Vice President of Research and Development and Chief Medical Officer	Vice President, Xcyte Therapies; Assistant Professor, Division of Hematology/Oncology at UCSF. Dr. Frohlich received his B.S. from Yale University in electrical engineering and economics and his M.D. from Harvard Medical School.
John E. Osborn	Executive Vice President and General Counsel	Executive Vice President and General Counsel, US Oncology, Inc.; Executive Vice President and General Counsel, Cephalon, Inc. Mr. Osborn is a graduate of the University of Iowa, and earned a law degree from the University of Virginia and a master's in international public policy from Johns Hopkins.
Richard J. Ranieri	Executive Vice President of Human Resources	Executive Vice President—Human Resources, Sepracor, Inc.; Senior Vice President—Human Resources and Chief Administrative Officer, Neurocrine Biosciences. Mr. Ranieri received an M.S. from Rider College and a B.A. from Villanova University.
Gregory T. Schiffman	Executive Vice President and Chief Financial Officer	Executive Vice President and Chief Financial Officer, Affymetrix; Vice President and Controller, Applied Biosystems; Divisional Manufacturing Manager and Controller, Hewlett Packard. Mr. Schiffman holds an M.B.A. from the Kellogg School of Business at Northwestern University and a B.S. in accounting from DePaul University.
David L. Urdal, Ph.D.	Executive Vice President and Chief Scientific Officer	President, Immunex Manufacturing Corporation; Vice President and Director—Development, Immunex Corporation. Dr. Urdal received a B.S. and an M.S. in public health and a Ph.D. in biochemical oncology from the University of Washington.

Sources: Dendreon Corporation and William Blair & Company, L.L.C.

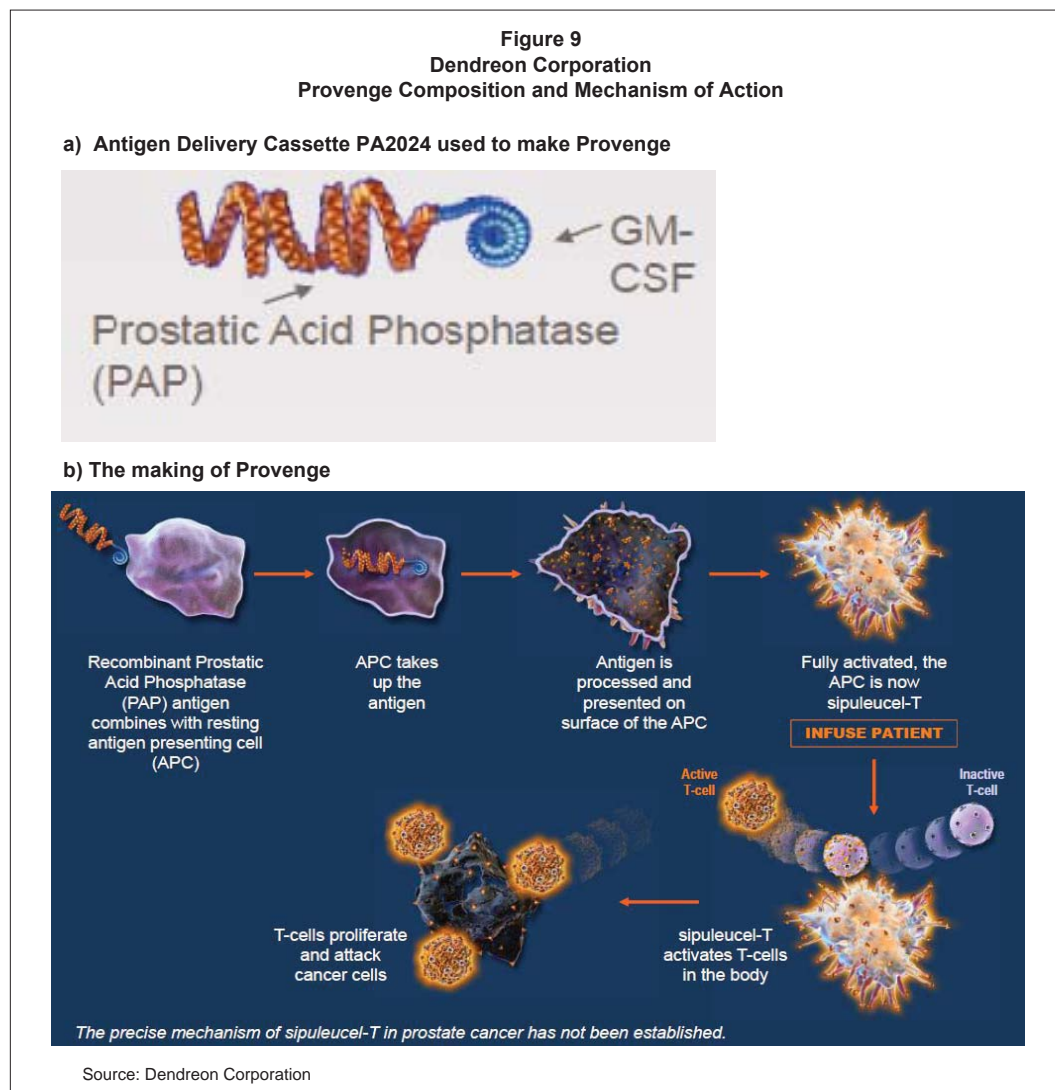
Summary of Provenge (Sipuleucel-T): An Autologous Cellular Immunotherapy

Provenge is an autologous (patient's own) cellular vaccine, made with a patient's own antigen-presenting cells (APCs) and activated by a proprietary antigen *ex vivo* (outside the body). When the activated APCs are reinfused into the patient, they activate antigen-specific T cells that subsequently attack the prostate cancer cells.

The underlying technology for Provenge, as well as Dendreon's other engineered cancer vaccines, is the *ex vivo* activation of APCs, mostly dendritic cells, with the company's proprietary Antigen Delivery Cassette (ADC) technology. The ADC is a three-region protein composed of: 1) an enhanced dendritic cell-binding region; 2) an antigen-processing region, specific for T cell activation; and 3) the engineered antigen. The dendritic cell-binding region is common to all ADCs, while the antigen processing and antigen regions vary depending on the particular target.

The antigen: PA2024, a fusion protein of GM-CSF and PAP. For Provenge, the specific tumor-associated antigen used in the ADC is PA2024, a recombinant fusion protein consisting of the human granulocyte-macrophage colony-stimulating factor (GM-CSF) linked to human prostatic acid phosphatase (PAP).

GM-CSF is a well-known cytokine responsible for the stimulation of white blood cells, specifically granulocytes (neutrophils, eosinophils, and basophils) and monocytes. PAP, a tyrosine phosphatase, is highly expressed in 95% of prostate cancer cells.

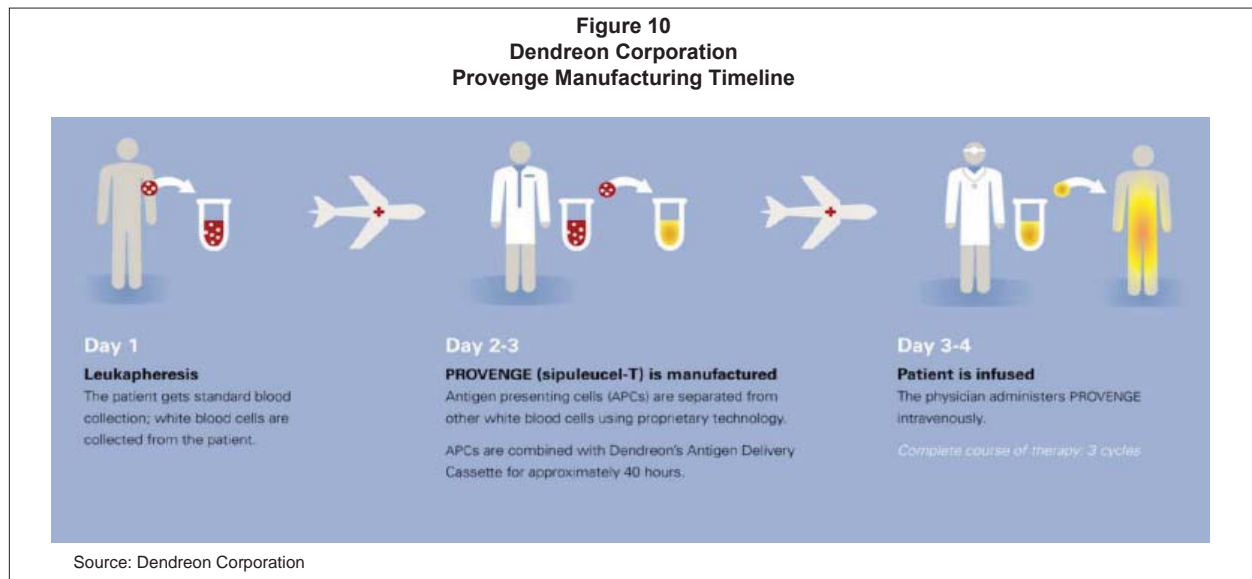


Making Provenge. The patient first undergoes a round of leukopheresis at his oncologist's or urologist's office; the process selectively separates and removes leukocytes (white blood cells) from the peripheral blood, while returning whole blood to the patient.

Upon receipt of the patient's leukocytes, Dendreon uses a proprietary technology to separate out the APCs, which include dendritic cells, macrophages, and B cells, from other leukocytes collected during the leukopheresis. The selected APCs are then incubated with PA2024-loaded ADCs for roughly 36-40 hours. The fully activated APCs become Provenge. Each dose of Provenge must contain a minimum of 50 million CD54-positive cells to pass release specifications. CD54, also known as intercellular adhesion molecule 1, is expressed on APCs, and plays an important role in binding and activating T cells. It has been shown that there is a strong correlation between cumulative CD54 upregulation and overall survival (Higano et al., *Cancer* 2009; 115:3670-9).

Following quality inspection, the patient's Provenge is shipped to the prescribing physician to be infused into the patient within 18 hours. Provenge then activates the body's T cells, which attack the tumor cells.

In total, the process to manufacture, deliver, and administer a dose of Provenge takes three to four days (figure 10). A complete course of therapy includes three cycles of Provenge given at days 0, 14, and 28.



Logistics of the supply chain. Dendreon has three manufacturing facilities located in New Jersey (48 workstations), Atlanta (36 workstations), and Los Angeles (36 workstations). All three facilities are up and running. Dendreon implements its proprietary Intellivenge system to manage the logistics of the sophisticated supply chain.

Summary of Provenge Phase III Clinical Programs

In early 2000, Dendreon commenced its late-stage development strategy for Provenge with the initiation of the D9901 and D9902 Phase III studies. D9902 was eventually segmented into D9902A and D9902B (IMPACT) studies. IMPACT officially began enrolling patients in August 2003, and positive results were released in April 2009.

The decade-long roller coaster ride for the company included a positive vote by the Cellular, Tissue, and Gene Therapies Advisory Committee in March 2007, the approvable letter from the FDA two months later, and lastly, regulatory approval of an amended biologics license application (BLA) in April 2010.

We summarize the timeline of the Phase III development and regulatory milestones for Provenge over the past decade in table 10.

Approval of Provenge for the treatment of metastatic prostate cancer was predicated on the safety and efficacy of three randomized, placebo-controlled Phase III studies—D9901, D9902A, and IMPACT—in mCRPC patients with no or minimal symptoms. Survival results across the three Phase III randomized sipuleucel-T studies are highlighted in table 2, on page 12. A Phase II study, called P-11 or PROTECT, evaluated Provenge in patients with hormone-sensitive prostate cancer, an earlier setting to mCRPC. We review the largest Phase III study, IMPACT, below.

Table 10
Dendreon Corporation
Provenge Development and Regulatory Timeline

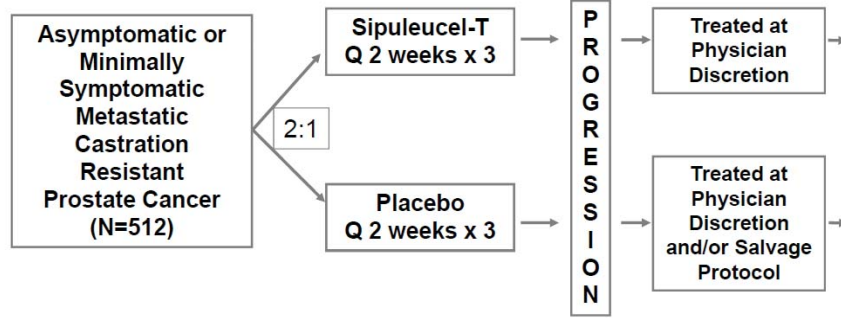
Date	Study	Milestone
January 2000	D9901	Study initiated—asymptomatic metastatic Hormone-Refractory Prostate Cancer (HRPC)
May 2000	D9902	Study initiated—asymptomatic metastatic Hormone-Refractory Prostate Cancer (HRPC)
September 2001	P-11 (PROTECT)	Study initiated—non-metastatic Androgen-Dependent Prostate Cancer (ADPC)
August 2002	D9901	Data—Fails to meet primary endpoint (time-to-disease progression [TTP])
October 2002	D9902A	Study amended—D9902A to include subjects already enrolled in D9902, regardless of Gleason score
August 2003	D9902B (IMPACT)	Study initiated—D9902B to include metastatic HRPC patients with a Gleason score of 7 or lower
October 2004	D9901	Data—Statistically significant three-year survival benefit observed (log-rank test); however, survival analysis was not prespecified
January 2005	D9902A	Data—Fails to meet primary endpoint (time-to-disease progression [TTP])
July 2005	D9902A	Data—Reports secondary endpoint three-year survival benefit; log-rank test (not s.s.), Cox multivariate (s.s.)
November 2005	D9902B (IMPACT)	Study amended—Patients eligible regardless of Gleason score, primary endpoint becomes Overall Survival (OS)
November 2006	P-11 (PROTECT)	Data—Fails to meet primary endpoint [(Time to biochemical failure [BF]); Meets secondary endpoint (PSA doubling time [PSADT])
November 2006		Dendreon submits BLA for Provenge
January 2007		FDA grants priority review for Provenge
March 2007		Cellular, Tissue, and Gene Therapies Advisory Committee—13-to-4 vote in favor of efficacy, 17-to-0 vote in favor of safety
May 2007		Dendreon receives Approvable Letter from FDA—Agency requests additional data to support efficacy and CMC process
April 2009	D9902B (IMPACT)	Data—Meets primary endpoint (statistically significant improvement in overall survival [OS])
November 2009		Dendreon submits amended biologics license application
April 2010		FDA Approves Provenge for the treatment of asymptomatic or minimally symptomatic metastatic CRPC
s.s.: statistically significant		
Sources: Dendreon Corporation and William Blair & Company, L.L.C.		

The IMPACT Study

Study design: Overall survival is primary endpoint. From August 2003 through November 2007, 512 men with CRPC were enrolled in the pivotal multicenter Phase III IMPACT study. Patients were randomly assigned in a 2-to-1 ratio to either the sipuleucel-T cohort (n=341) or the placebo cohort (n=171). Similar to the previous studies, patients received treatment intravenously every two weeks for a total of three infusions (see figure 11, on the following page).

Distinct from the earlier Phase III studies, D9901 and D9902A, the primary endpoint for the IMPACT study was overall survival. The secondary endpoint of the study was time-to-objective-disease progression (ODP), which was assessed by CT and bone scans at prespecified points.

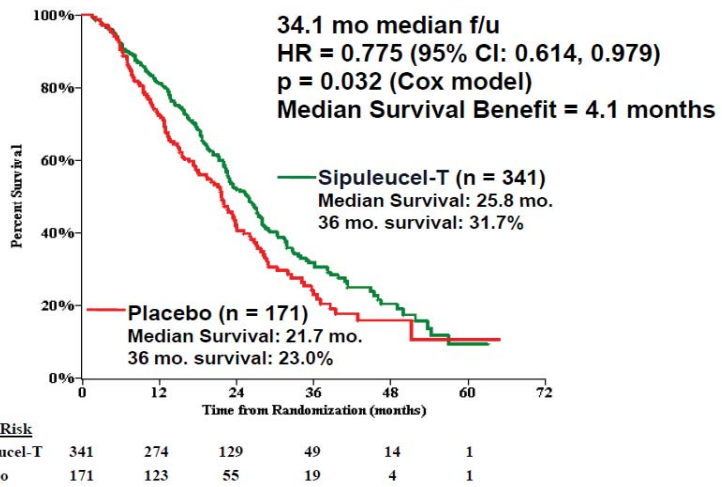
Figure 11
Dendreon Corporation
Phase III Impact Study Design



Sources: Kantoff ASCO-GU 2010, and Dendreon Corporation

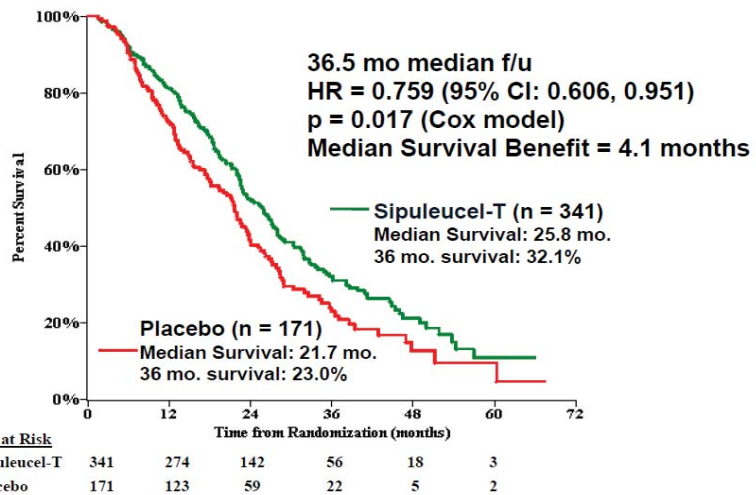
Figure 12
Dendreon Corporation
Kaplan-Meier Estimates for Impact Primary Endpoint—Overall Survival

a) Primary Analysis (331 events)



Sources: Kantoff ASCO-GU 2010, and Dendreon Corporation

b) Final Analysis (349 events)



Sources: Kantoff ASCO-GU 2010, and Dendreon Corporation

IMPACT meets primary endpoint of overall survival. Announced in April 2009, top-line data showed that the sipuleucel-T cohort had an overall improvement in median survival benefit of 4.1 months, when compared with placebo (25.8 months versus 21.7 months). This translated into a relative reduction of 22% in the risk of death compared with placebo: hazard ratio (HR) = 0.775 (95% confidence interval: 0.614, 0.979); p=0.032. The 36-month survival probability for the sipuleucel-T arm was 31.7%, compared with 23.0% for the placebo arm.

The final analysis, based on 349 events from the study closure date, confirmed the previously reported 4.1-month median survival benefit for the sipuleucel-T cohort: HR = 0.759, p=0.017. A slightly increased 36-month survival probability of 32.1% for the sipuleucel-T was also reported at the final analysis.

Secondary endpoint of disease progression again not impactful. Independent analysis of the secondary endpoint for the IMPACT study, as determined by a blinded radiology review committee, concluded that time-to-objective-disease progression (time to ODP) was similar between the two study arms. The median time to ODP was 14.6 weeks (3.7 months) and 14.4 weeks (3.6 months) for the Provenge and placebo cohorts, respectively; HR= 0.951, p=0.628. The same findings were concluded from the earlier Phase III studies.

Good safety. In general, Provenge was well tolerated, and the majority of patients in the IMPACT study received all three infusions of treatment. Adverse events more commonly reported in the Provenge group included chills, pyrexia, headache, flu-like symptoms, and myalgia (table 11). Most events were grade 1 or 2, occurred typically one day after infusion, and were resolved after a few days. Importantly, there was no increase of incidence of cerebrovascular events in the Provenge cohort when compared with placebo, an observation previously reported from the integrated data analysis of the D9901 and D9902A studies.

Table 11
Dendreon Corporation
Common Adverse Events From Phase III Impact Study

	Sipuleucel-T N=338	Placebo N=168
Adverse Events, %		
Rigors (chills)	54.1%	12.5%
Pyrexia	29.3%	13.7%
Headache	16.0%	4.8%
Influenza-like illness	9.8%	3.6%
Myalgia	9.8%	4.8%
Hypertension	7.4%	3.0%
Hyperhidrosis	5.3%	0.6%
Groin pain	5.0%	2.4%

† Reported by ≥ 5% of sipuleucel-T patients and having a ≥ 2-fold difference from placebo

Sources: Kantoff ASCO-GU 2010, and Dendreon Corporation

Table 12
Dendreon Corporation
Income Statement
(dollars in thousands)

	2009A	2010A	2011E				FY:11E	2012E FY:12E	2013E FY:13E
			Q1A	Q2A	Q3E	Q4E			
Revenues									
Provenge—United States	\$0	\$48,036	28,061	49,555	65,082	71,147	221,564	368,622	548,794
Provenge—European Union	-	-	-	-	-	-	-	-	2,405
Collaboration revenue	101	21	-	-	-	-	-	-	-
Total Revenues	101	48,057	28,061	49,555	65,082	71,147	213,845	368,622	551,198
Expenses									
COGS	-	28,520	18,338	28,754	36,446	38,419	121,957	189,416	274,397
R&D expense	61,586	75,941	17,609	18,565	18,936	19,315	74,425	79,995	83,243
SG&A expense	38,556	235,760	95,289	105,071	61,063	52,212	313,635	219,501	239,066
Total Operating Expenses	100,142	340,221	131,236	152,390	116,446	109,946	510,018	488,912	596,707
Operating income	(100,041)	(292,164)	(103,175)	(102,835)	(51,364)	(38,799)	(296,173)	(120,290)	(45,508)
Interest income/(expense), net	964	1,144	400	393	312	243	1,348	668	365
Other income/(expense), net	(2,321)	(1,588)	(8,993)	(12,147)	(14,606)	(6,208)	(41,954)	(41,628)	(40,970)
Gain (loss) from valuation of warrant liability	(118,763)	(142,567)	-	-	-	-	-	-	-
Loss on debt conversion	-	(4,716)	-	-	-	-	-	-	-
Restructuring costs	-	-	-	-	(21,000)	(2,100)	(23,100)	-	-
Pretax income/(loss)	(220,161)	(439,891)	(111,768)	(114,589)	(86,658)	(46,863)	(359,878)	(161,250)	(86,114)
Provision for income taxes/(income)	-	(411)	-	-	-	-	-	-	-
GAAP Net Income/(Loss)	(\$220,161)	(\$439,480)	(\$111,768)	(\$114,589)	(\$86,658)	(\$46,863)	(\$359,878)	(\$161,250)	(\$86,114)
GAAP EPS	(\$2.04)	(\$3.18)	(\$0.77)	(\$0.79)	(\$0.59)	(\$0.32)	(\$2.47)	(\$1.10)	(\$0.58)
Weighted average shares outstanding, diluted	108,050	138,206	145,494	145,928	146,028	146,128	145,895	146,503	147,228

Sources: Dendreon Corporation and William Blair & Company, L.L.C. estimates

Table 13
Dendreon Corporation
Balance Sheet
(dollars in thousands)

	2009A	2010A	2011E					2012E FY:12E	2013E FY:13E
			Q1A	Q2A	Q3E	Q4E	FY:11E		
Current assets									
Total cash, cash equivalents, short-term investments	\$576,945	\$254,791	\$712,391	\$623,663	\$486,870	\$422,887	\$422,887	\$231,384	\$129,684
Restricted cash	-	-	-	-	-	-	-	-	-
Trade accounts receivable	-	12,679	16,864	28,039	36,446	39,131	39,131	36,727	52,719
Prepaid antigen costs	18,975	17,656	24,325	19,570	21,570	23,570	23,570	31,570	39,570
Inventories	-	30,928	38,872	52,265	61,828	64,032	64,032	83,948	96,400
Prepaid expense and other	8,566	14,340	21,925	30,194	30,194	30,194	30,194	30,194	30,194
Total current assets	604,486	330,394	814,377	753,731	636,907	579,814	579,814	413,823	348,567
Property, plant and equipment, net	98,964	246,889	244,206	248,822	283,822	294,822	294,822	299,822	309,822
Long-term investments	29,441	22,505	66,630	50,284	50,284	50,284	50,284	50,284	50,284
Long-term restricted cash	-	-	-	-	-	-	-	-	-
Debt issuance costs and other assets	2,524	4,165	5,475	5,569	5,569	5,569	5,569	5,569	5,569
Total assets	735,415	603,953	1,130,688	1,058,406	976,582	930,489	930,489	769,498	714,242
Current liabilities									
Accounts payable	2,257	7,847	11,980	7,308	5,822	5,497	5,497	6,464	8,041
Accrued liabilities	19,557	19,842	21,355	33,213	33,213	33,213	33,213	33,213	33,213
Accrued compensation	6,855	17,410	15,727	15,461	15,461	15,461	15,461	15,461	15,461
Convertible senior Notes, due 2016	-	-	491,424	496,974	502,524	508,074	508,074	530,274	552,474
Deferred revenue	-	-	-	-	-	-	-	-	-
Warranty liability	132,953	-	-	-	-	-	-	-	-
Current portion of capital lease obligations	722	4,045	3,818	3,813	3,813	3,813	3,813	3,813	3,813
Current portion of facility lease obligations	592	935	948	966	966	966	966	966	966
Current portion of long-term debt	-	-	-	-	-	-	-	-	27,685
Total current liabilities	162,936	50,079	545,252	557,735	561,800	561,800	561,800	556,978	608,441
Long-term accrued liabilities	1,554	6,760	6,840	6,920	6,920	6,920	6,920	6,920	6,920
Deferred revenue, net of current	-	-	-	-	-	-	-	-	-
Capital lease obligations, net of current	706	7,099	5,124	11,855	11,855	11,855	11,855	11,855	11,855
Facility lease obligation, net of current	14,120	19,556	19,336	19,087	18,857	18,627	18,627	17,707	16,787
Convertible senior subordinated notes	52,535	27,685	27,685	27,685	27,685	27,685	27,685	27,685	-
Total liabilities	231,851	111,179	604,237	623,282	627,117	626,887	626,887	621,145	644,003
Stockholders' equity	503,564	492,774	526,451	435,124	349,466	303,603	303,603	148,353	70,239
Total liabilities and stockholders' equity	735,415	603,953	1,130,688	1,058,406	976,582	930,489	930,489	769,498	714,242

Sources: Dendreon Corporation and William Blair & Company, L.L.C. estimates

Table 14
Dendreon Corporation
Statement of Cash Flows
(dollars in thousands)

	2009A	2010A	2011E	2012E	2013E
Net cash from operating activities					
Net Income (Loss)	(\$220,161)	(\$439,480)	(\$359,878)	(\$161,250)	(\$86,114)
Adjustments					
Stock-based compensation	17,212	40,262	42,687	41,929	41,900
Depreciation and amortization expense	4,662	16,084	44,223	23,986	24,786
Warranty liability gain/(loss)	118,763	142,567	-	-	-
Amortization of securities discount and premiums	648	1,540	2,500	-	-
Amortization of convertible notes discount and debt issuance costs	-	-	21,692	21,692	21,692
Loss on conversion of debt	-	4,716	-	-	-
Other	-	1,623	1,250	-	-
Change in Operating Assets and Liabilities					
Accounts receivable	-	(12,679)	(26,452)	2,404	(15,991)
Inventories	-	(17,054)	(33,104)	(19,916)	(12,452)
Prepaid antigen costs	(18,975)	(10,673)	(5,914)	(8,000)	(8,000)
Prepaid expenses	(6,466)	(10,722)	(15,854)	-	-
Restricted cash related to operating lease	-	-	(1,404)	-	-
Accounts payable	2,020	5,590	(2,350)	967	1,577
Accrued liabilities and compensation	16,856	10,840	11,422	-	-
Deferred collaboration revenue	(82)	(82)	-	-	-
Net cash used in operating activities	(85,523)	(267,468)	(321,182)	(98,188)	(32,601)
Cash flows from investing activities					
Purchase of property and equipment	(216,094)	(140,761)	(47,933)	(5,000)	(10,000)
Purchases of investments	(65,912)	(312,064)	(200,000)	(100,000)	(250,000)
Maturities of investments	69,894	362,713	100,000	100,000	200,000
Net cash used in (provided by) investing activities	(212,112)	(90,112)	(147,933)	(5,000)	(60,000)
Cash flows from financing activities					
Proceeds from issuance of convertible debt, net	-	-	607,129	-	-
Proceeds from sale of equity securities, net	630,305	-	-	-	-
Proceeds from issuance of warrants	-	71,360	-	-	-
Proceeds from release of debt security deposits	3,853	112	-	-	-
Payments on long-term debt	(2,194)	-	-	-	-
Payments on facility lease obligation	(194)	(685)	(500)	-	-
Payments on capital lease obligations	(365)	(1,959)	(3,500)	-	-
Proceeds from exercise of stock options	14,936	7,511	6,000	6,000	8,000
Proceeds from issuance of common stock, ESSP	1,600	4,407	4,800	1,200	1,600
Net cash provided by financing activities	647,941	80,746	613,929	7,200	9,600
Cash balance (Beginning of Period)	59,523	409,829	132,995	277,809	181,821
Difference	350,306	(276,834)	144,814	(95,988)	(83,001)
Cash balance (End of Period)	409,829	132,995	277,809	181,821	98,819
Marketable securities	167,116	121,796	145,078	49,563	30,865
Cash balance plus marketable securities (end of period)	576,945	254,791	422,887	231,384	129,684

Sources: Dendreon Corporation and William Blair & Company, L.L.C. estimates

Medivation, Inc.

A Rising Star in Prostate Cancer Therapeutics

We are initiating coverage of Medivation with an Outperform rating and a 12-month price target of \$35.

We believe that Medivation's lead asset, MDV3100, partnered with Astellas, is one of the most promising candidates for prostate cancer in today's competitive landscape. MDV3100 is a next-generation anti-androgen agent, currently in two Phase III studies in metastatic castration-resistant prostate cancer (mCRPC): AFFIRM in the post-chemotherapy setting and PREVAIL in the chemo-naïve setting. Two Phase II studies are also ongoing, which are testing MDV3100 upstream on the disease continuum in hormone-sensitive settings.

Strong catalyst coming before the end of 2011: the interim analysis of AFFIRM. Positive data could lead to NDA filing and potential approval in 2012; we assign 75% probability for success. Medivation and Astellas decided to conduct an interim analysis of the AFFIRM study, which appears to be overpowered based on the experience gained from the successful Phase III study of Zytiga in the same setting. Based on the mechanism of action and prior clinical data of MDV3100, we believe there is a good chance the study will be successful.

Our probability-adjusted NPV analysis suggests a \$35 price target. In our model, we assume worldwide peak sales for MDV3100 at \$2.2 billion, 75% probability of reaching the market, 50% share in the United States, and 15% royalty on non-U.S. sales. This valuation accounts for MDV3100 in the mCRPC settings tested in the two Phase III studies only.

A free option lies in dimebon in Alzheimer's disease; Phase III CONCERT data expected in first half 2012. Before MDV3100 rose to prominence in Medivation's pipeline, dimebon was the lead asset in Alzheimer's disease (AD) and Huntington's disease (HD). Despite one strikingly positive study in AD, all subsequent studies in AD and HD failed or were discontinued, leaving CONCERT as the only study running. The chance for the success of this study is low, and we do not include it in our valuation. Still, should this study be successful, the stock could offer substantial upside, which we estimate at roughly \$20 per share.

Medivation, based in San Francisco, California, is a biopharmaceutical company focused on the Phase III development of novel therapeutics for prostate cancer. Its lead asset, MDV3100, is in Phase III studies.

Healthcare | Biotechnology

Stock Rating: **Outperform**
Company Profile: **Aggressive Growth**
Price Target: **\$35**

Symbol: MDVN (NASDAQ)
Price: \$18.91 (52-Wk.: \$11-\$26)
Market Value (mil.): \$660.7
Fiscal Year End: December
Dividend Yield: None

Estimates

	2010A	2011E	2012E
EPS FY	(\$0.99)	(\$1.18)	(\$1.26)
Sales (mil.)	\$62.5	\$62.1	\$71.4

Valuation

FY P/E	NM	NM	NM
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Trading Data

Shares Outstanding (mil.)	34.9
Float (mil.)	33.2
Average Daily Volume (thous.)	498.6

Financial Data

Total Debt/Total Capital	NM
Enterprise Value (mil.)	\$471.6
Price/Sales	10.7

Investment Summary

We Believe MDV3100 Is One of the Most Promising Candidates in Prostate Cancer

MDV3100 is an anti-androgen inhibiting the activation of the androgen receptor (AR). Because the AR pathway is well validated in driving prostate cancer growth, we believe the risk for development is lower for MDV3100 compared with other candidates with novel mechanisms of action. MDV3100 blocks the AR activation process at three distinct steps: competitively binding to AR, inhibiting translocation to the nucleus, and preventing DNA binding inside the nucleus (figure 4b, on page 9). Compared with the most used anti-androgen Casodex (\$1.3 billion in sales in 2008), MDV3100 1) has 8 times higher affinity to the AR; 2) can overcome AR mutations resistant to Casodex; and 3) appears to be a true AR antagonist as opposed to Casodex, which has partial AR agonism resulting in weakened efficacy.

Two Phase III studies ongoing; AFFIRM study in the post-chemo setting and PREVAIL in the frontline setting, both in mCRPC. We outline the study timeline and design in table 3, on page 15. Data from AFFIRM is due out in 2012, with an interim analysis before year-end 2011. Data from PREVAIL will likely be available during 2014 (see figure 3, on page 6).

Two Phase II studies are ongoing, both in hormone-sensitive prostate cancer. One such study is MDV3100 versus Casodex, and the other study is in ADT-naive patients (those not yet exposed to androgen deprivation therapy [ADT]). These studies will explore utilities of MDV3100 earlier in the disease continuum. There are 5-10 times more eligible patients for MDV3100 in the earlier setting than in the mCRPC setting.

Our probability-adjusted NPV model values Medivation at \$35 per share. As detailed below, in our model we assume worldwide peak sales of \$2.2 billion, 75% probability of reaching the market, 50% share in the United States, and 15% royalty on non-U.S. sales.

History and IP. In September 2005, Medivation licensed the MDV3100 series of compounds, including MDV3100, from University of California, Los Angeles. Full details of the agreement were not disclosed; however, management has indicated that UCLA is entitled to low-single-digit royalties from future sales of MDV3100. Earlier in 2010, Medivation announced the issuance of MDV3100's composition-of-matter patent from the United States Patent and Trademark Office. Protection for MDV3100 runs through 2027; a potential extension of five years is possible based on MDV3100's development time frame.

The Astellas Partnership on MDV3100, Established in October 2009

Comprehensive development program in prostate cancer. MDV3100 was to be studied in both mCRPC and earlier-stage hormone-sensitive prostate cancer.

Terms. The agreement called for Astellas to pay Medivation \$110 million in up-front payment, and an additional \$655 million in milestones with \$320 million at pre-launch stages. Astellas is responsible for two-thirds of development costs, while Medivation bears the rest. Medivation is entitled to 50% profits in the United States and tiered double-digit royalties on non-U.S. sales.

AFFIRM Interim Analysis Before the End of 2011; We Expect Data to Be Comparable to Abiraterone

Rationale and statistical requirement for the interim analysis. AFFIRM enrolled 1,199 mCRPC patients, with the primary endpoint overall survival (OS). The AFFIRM design is practically identical to the successful COU-AA-301 study of abiraterone in the post-Taxotere setting. Because abiraterone and MDV3100 both target the AR pathway, and their Phase I/II data in this setting were comparable, we believe there is a good chance for MDV3100 to be successful in this study.

We summarize the design, pre-specified number of death events for interim and final analyses, and associated statistical assumptions in table 15.

Table 15
Medivation, Inc.
Comparison of Design, Interim and Final Analysis, and Statistical Assumptions
Between COU-AA-301 and AFFIRM

	Phase III Study	
	COU-AA-301	AFFIRM
Investigative agent	Zytiga (abiraterone) + prednisone	MDV3100
Enrolled patients	1,195	1,199
Active agent: placebo randomization ratio	2:1	2:1
Prespecified number of deaths required for final analysis	797	786
Modified number of deaths required for final analysis	--	650
Number of deaths for interim analysis	534	520
Ratio of numbers of deaths, interim analysis vs. final analysis	0.67	0.80
Required p-value for statistical significance evaluation at interim	0.012	0.024
Actual p-value for the interim analysis	<0.001	To be released YE:11

Sources: Company reports and William Blair & Company, L.L.C. estimates

Based on the experience of COU-AA-301, where the interim analysis was conducted at 534 events and the p value achieved was less than 0.001, Medivation and Astellas decided to conduct the interim analysis at 520 events. Further, Medivation and Astellas modified pre-specified number of deaths required for final analysis from 786 to 650; this way the p value required at the interim analysis is 0.024, versus abiraterone's at 0.012, effectively lowering the statistical hurdle for the interim analysis to be successful. In addition, lowering the number of events for the final analysis will also allow the final analysis to follow the interim analysis more quickly, minimizing complications.

In Frontline mCRPC, MDV3100 Could Produce Better Data than Abiraterone

While the data is comparable in the post-chemo setting between the two agents, in the pre-chemo setting MDV3100 has demonstrated much better time to PSA progression (TTPP) compared with abiraterone (60 weeks versus 32 weeks). In patients who were ketoconazole naive, TTPP was 116 weeks for MDV3100 and 71 weeks for abiraterone. Time to radiologic progression also appeared impressive, at 56 weeks for MDV3100; although the corresponding data for abiraterone in its Phase I/II study has not been reported, in Provenge pivotal studies, the time to progression was roughly 14.5 weeks (table 4, on page 17).

As shown in figure 4, abiraterone acts to block synthesis of androgens, while MDV3100 works at the androgen-receptor level to block the signaling pathway. MDV3100 may be viewed as acting downstream of abiraterone in the AR signaling pathway. Further, the prostate cancer disease at the pre-chemo setting is more AR pathway-dependent than in the post-chemo setting. Together, this might explain why MDV3100, compared with abiraterone, appears more effective in the pre-chemo setting while similar in the post-chemo setting.

If PREVAIL produces better progression-free survival (PFS) and overall survival (OS) data than COU-AA-302, MDV3100 will garner higher market share in this setting.

Contamination Risks to PREVAIL Appear to Be Under Control

The PREVAIL study is currently enrolling—trailing abiraterone by 15 months. Patients who progress on MDV3100 might cross over to abiraterone or other agents, potentially compromising the OS data.

We believe such risks are being minimized by the following factors: 1) most PREVAIL clinical sites are in the EU, where abiraterone is launched later than in the United States; 2) PREVAIL is a much larger study with a target enrollment of 1,680 versus 1,000 for COU-AA-302, enhancing the power of the study; and 3) since MDV3100 might be more effective in this setting than abiraterone, even if placebo patients on PREVAIL cross over to abiraterone after progression, the effect would probably not be strong enough to crash the study.

MDV3100 Could Eventually Move to Front Line

Two Phase II studies ongoing. Medivation and Astellas are moving MDV3100 to earlier stage, hormone-sensitive disease. The Phase II, 370-patient TERRAIN study examines MDV3100 head-to-head against Casodex in patients who have progressed following medical castration with LHRH or surgical castration. The primary endpoint is PFS.

The companies also initiated another Phase II study in May 2011 to evaluate MDV3100 as a first-line treatment in patients who are hormone naive without prior medical or surgical castration. The study aims to enroll 60 patients in Europe, and the study duration is 24 weeks.

Strategy: Compendia listing or formal label expansion. If AFFIRM and PREVAIL succeed and MDV3100 garners approvals in two mCRPC settings in the 2012-2015 time frame, the TERRAIN and other Phase II study data could be included in the compendia listing and enable MDV3100's use in the hormone sensitive settings. Medivation and Astellas may or may not need to conduct large Phase III studies to formally expand the label if the compendia listings are well accepted and practiced.

Pricing. We expect MDV3100 to be priced at a comparable level to abiraterone, which is \$5,000 per month, although better data in the frontline mCRPC setting could command a premium. As MDV3100 moves into the hormone-sensitive stage, the price could decrease; however, the expansion of the addressable patient population and longer treatment duration will make up for the price decrease, resulting in a larger overall opportunity.

Dimebon Is a Free Option, after the High-Profile Failure of the Phase III CONNECTION Study in Alzheimer's Disease

Proposed mechanism of action. Dimebon is an antihistamine, but was also shown to stabilize mitochondrial membrane function and induce neurite outgrowth in vitro. As synapse loss and mitochondrial dysfunction are hallmarks of AD and HD, dimebon may function as a neuroprotector and a booster of cellular energy, which could affect progression of neurodegenerative diseases, in general.

Successful Russian monotherapy study in AD. The first dimebon study in AD was conducted in Russia. Naive mild-to-moderate AD patients received dimebon or placebo for a six-month treatment period. At week 26, dimebon demonstrated a statistically significant benefit in ADAS-cog scores (Alzheimer's Disease Assessment Scale-cognitive subscale, $p < 0.0001$). Dimebon's treatment effect over placebo also continued for more than one year.

High-profile failure of CONNECTION in March 2010. The CONNECTION study design was virtually identical to the Russian study, but the study was conducted in the United States, Europe, and South America. Top-line data released in March 2010 showed that dimebon was no different than placebo in these patients, on all five endpoints including ADAS-cog.

Keeping *CONCERT* and dropping *CONTACT* and *CONSTELLATION* in AD. Following the failure of *CONNECTION*, Medivation and partner Pfizer decided to focus resources on studies that have the highest chance of success, given the current understanding and working hypotheses. The companies stopped enrollment in *CONTACT* and *CONSTELLATION*, two Phase III studies in moderate-to-severe AD, but kept *CONCERT*, which studies dimebon add-on to Aricept for a 12-month duration in mild-to-moderate AD patients. The *CONCERT* population is a more real-life population than that in *CONNECTION* (dimebon monotherapy in naive mild-to-moderate AD), as most patients in the United States and Europe are on Aricept already. Further, treating early diseases has a higher chance to demonstrate a treatment effect than treating later-stage diseases, in our opinion. *CONCERT* top-line data is due out in early 2012.

Failure of *HORIZON* in HD in April 2011. *HORIZON* missed both the co-primary endpoints of Mini-Mental State Examination (MMSE, $p=0.39$), and the Clinician's Interview-Based Impression of Change, plus caregiver input (CIBIC-plus, $p=0.84$).

Probability of success of *CONCERT* is low, and we do not include dimebon in our valuation.

History and IP. Dimebon is an antihistamine that has been marketed in Russia for more than 20 years. In October 2003, Medivation licensed worldwide rights to dimebon for the treatment of neurodegenerative diseases from Selena Pharmaceuticals for \$25,000 in cash and an equity stake in Medivation. The licensing terms are favorable; there is a lifetime cap of \$5 million in milestones, and the royalty rate is 0.5%. The method-of-use patents of dimebon in neurologic diseases expire in 2016 plus five years under the Hatch-Waxman Act.

The Pfizer Partnership on Dimebon, Established in September 2008

Terms. The agreement called for Pfizer to pay Medivation \$225 million in up-front payment, an additional \$500 million in prelaunch milestones, and significant post-launch milestones. Pfizer is responsible for 60% of development costs in the United States and 100% outside the United States, while Medivation bears 40% of the costs in the United States. Medivation is entitled to 40% profits in the United States as well as royalties on non-U.S. sales. The agreement does not include follow-on compounds to dimebon that Medivation has developed.

Risks to Our Outperform Rating

Risks to our Outperform rating and attainment of our price target for Medivation include failure to meet efficacy endpoints for the Phase III programs of MDV3100, unforeseen safety issues of MDV3100 in longer-term studies, failure in efficacy of dimebon in Phase III programs in Alzheimer's disease, setbacks in clinical and business development, and financing risk.

Valuation

In building the probability-adjusted net present value (NPV) model, we estimate the peak sales of a particular drug candidate, its probability of advancing to the next stage of development and eventually reaching the market, and the company's share of revenue and expenses depending on the commercialization plan and/or structure of any partnerships. We then calculate the cash flows after adjusting all revenues and expenses with respective cumulative probabilities for each stage. The cash flows are discounted back using an industry-specific weighted average cost of capital (WACC) of 12% to arrive at a probability-adjusted NPV for each drug candidate. Once we determine the NPV for each candidate, we then add net cash and other costs, which include expenses not directly associated with the development of the clinical candidates, to arrive at a fair value estimate for the stock.

For MDV3100, we assume worldwide peak sales of \$2.2 billion, 75% probability of reaching the market, 50% share in the United States, and 15% royalty on non-U.S. sales. As a result, our analyses value Medivation at \$35 per share (table 16).

Table 16
Medivation, Inc.
Sum-of-the-Parts Fair Value
(dollars in thousands)

Drug	Peak Sales	Stage of Development	Estimated Launch Date	Probability of Commercialization	Percentage of Sales to Company	Probability-Adjusted NPV	Value Per Share	Percentage of Fair Value
MDV3100—United States	\$1,283,328	Phase III	Q3:2012	75%	50:50 profit share with Astellas	\$1,040,959	\$29.21	83.7%
MDV3100—European Union	\$879,972	Phase III	Q1:2013	75%	15%	\$213,136	\$5.98	17.1%
Subtotal						\$1,254,095	\$35.20	100.9%
Net Cash at Year End 2012						\$6,967	\$0.20	0.6%
Net Present Value of Additional Gain (Loss)*						(\$17,857)	(\$0.50)	(1.4%)
Sum-of-Parts Fair Value						\$1,243,206	\$34.89	100.0%

Sources: Company reports and William Blair & Company, L.L.C. estimates

Management Team

Table 17
Medivation, Inc.
Brief Biographies of Management Team

Management	Position	Previous Experience
David Hung, M.D.	President and Chief Executive Officer	President and Chief Executive Officer, ProDuct Health, Inc; Vice President, Chiron Corporation
C. Patrick Machado, J.D.	Chief Business Officer and Chief Financial Officer	Senior Vice President & Chief Financial Officer, ProDuct Health, Inc; Vice President, Chief Financial Officer & General Counsel, ProDuct Health, Inc; Consultant, Cytoc Health Corporation
Lynn Seely, M.D.	Chief Medical Officer	Vice President, ProDuct Health, Inc; Vice President, Cytoc Health Corporation; Associate Director, Chiron Corporation
Cheryl Cohen	Chief Commercial Officer	President, CLC Consulting; Vice President—Strategic Commercial Group, Health Care Systems, Inc., a Johnson & Johnson company; Vice President—Rheumatology, Centocor, Inc., a Johnson & Johnson company

Sources: Medivation, Inc. and William Blair & Company, L.L.C.

Major Upcoming Catalysts Driving Value

We list the clinical development timeline and milestones for Medivation in table 18. Events that we expect to have a high impact on the stock are highlighted in brown. We expect the interim analysis of AFFIRM in late 2011, and final AFFIRM and CONCERT data in 2012, to drive value.

Table 18
Medivation, Inc.
Clinical Development Timeline/Milestones

Drug	MDV3100	Dimebon (latrepirdine)
Indication	Prostate Cancer	Alzheimer's disease
Class	Androgen Receptor (AR) antagonist	Mitochondrial Function Enhancer
Partner	Astellas	Pfizer
Q1:10		Results from Phase III CONNECTION study missed co-primary and secondary endpoints
Q2:10	Final Phase I/II results	Discontinued CONTACT and CONSTELLATION Phase III studies
Q3:10	Initiated Phase III PREVAIL study chemotherapy-naïve CRPC patients	
Q4:10		
Q1:11	Initiated Phase II TERRAIN study MDV3100 vs. Casodex (bicalutamide) (N=370, North America and Europe)	
Q2:11	Initiated Phase II study - ADT-naïve patients (N=60, Europe)	
Q3:11		
Q4:11	Phase III AFFIRM interim results (520 events; 80 percent of the 650 total events needed for the final analysis)	
Q1:12	NDA/MAA filing	
Q2:12		Phase III CONCERT results
Q3:12	Approval and Launch (post-chemo mCRPC)	NDA/MAA filing
Q4:12	Phase II study (ADT-naïve) results	
Q1:13		
Q2:13		
Q3:13	Phase II TERRAIN results	Approval and Launch
Q4:13	Potential Phase III PREVAIL interim results	

Brown highlight: Events likely to affect the stock price

Sources: Company reports and William Blair & Company, L.L.C. estimates

Table 19
Medivation, Inc.
Income Statement
(dollars in thousands)

Income statement	2009A	2010A	2011E				FY:11E	2012E	2013E
			Q1A	Q2A	Q3E	Q4E			
Revenues									
MDV3100 U.S. revenue	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$8,212	\$65,725
MDV3100 ex-U.S. royalties	-	-	-	-	-	-	-	-	1,523
Collaboration revenue	69,254	62,508	14,709	15,799	15,799	15,799	62,106	63,196	37,972
Total Revenues	69,254	62,508	14,709	15,799	15,799	15,799	62,106	71,408	105,220
Expenses									
COGS	-	-	-	-	-	-	-	493	3,944
R&D expense	87,728	72,228	17,618	19,139	20,096	20,498	77,351	86,174	90,991
SG&A expense	28,983	23,005	6,156	7,036	7,106	7,177	27,476	29,435	42,733
Total operating expenses	116,711	95,233	23,774	26,175	27,202	27,675	104,827	116,101	137,668
Operating income	(47,457)	(32,725)	(9,065)	(10,376)	(11,403)	(11,876)	(42,721)	(44,693)	(32,448)
Interest income/(expense), net	1,128	317	41	9	91	78	219	178	3
Other income/(expense), net	(152)	(57)	(333)	(99)	-	-	(432)	-	-
Pretax income/(loss)	(46,481)	(32,465)	(9,357)	(10,466)	(11,312)	(11,798)	(42,933)	(44,515)	(32,445)
Provision for income taxes/(income)	8,272	1,572	(905)	(992)	-	-	(1,897)	-	-
Net income/(loss)	(\$54,753)	(\$34,037)	(\$8,452)	(\$9,474)	(\$11,312)	(\$11,798)	(\$41,036)	(\$44,515)	(\$32,445)
GAAP earnings per share	(\$1.71)	(\$0.99)	(\$0.24)	(\$0.27)	(\$0.32)	(\$0.34)	(\$1.18)	(\$1.26)	(\$0.91)
Weighted average shares outstanding, diluted	32,094	34,290	34,663	34,888	34,963	35,038	34,888	35,226	35,588

Sources: Medivation, Inc. and William Blair & Company, L.L.C.

Table 20
Medivation, Inc.
Balance Sheet
(dollars in thousands)

Medivation, Inc.	2009A	2010A	2011					2012A	2013A
			Q1A	Q2A	Q3E	Q4E	FY:11E		
Balance sheet data									
Current assets									
Total cash, cash equivalents, short-term investments	\$278,244	\$207,756	\$194,959	\$182,361	\$156,355	\$129,863	\$129,863	\$6,967	(\$58,192)
Accounts receivable	6,490	21,188	14,747	14,763	14,763	14,763	14,763	14,763	16,763
Inventories	-	-	-	-	-	-	-	549	2,692
Prepaid expense and other	9,343	8,067	7,979	6,791	6,791	6,791	6,791	8,000	9,000
Total current assets	294,077	237,011	217,685	203,915	177,909	151,417	151,417	30,280	(29,737)
Property, plant and equipment, net	1,092	862	754	796	816	836	836	916	1,016
Restricted cash	843	843	843	843	843	843	843	843	843
Other noncurrent assets	678	887	1,785	2,760	2,760	2,760	2,760	2,760	2,760
Total assets	296,690	239,603	221,067	208,314	182,328	155,856	155,856	34,799	(25,118)
Current liabilities									
Accounts payable	4,840	3,229	4,879	6,285	6,285	6,285	6,285	6,285	7,285
Accrued expenses	12,054	21,399	21,704	24,201	24,201	24,201	24,201	24,201	25,701
Deferred revenue	86,570	59,153	59,216	59,762	59,762	59,762	59,762	59,762	21,790
Other current liabilities	800	5,193	453	459	459	459	459	459	459
Total current liabilities	104,264	88,974	86,252	90,707	90,707	90,707	90,707	90,707	55,235
Deferred revenue, net of current	166,598	141,507	126,735	113,390	97,591	81,792	81,792	-	-
Other non-current liabilities	554	1,438	1,412	1,296	1,296	1,296	1,296	1,296	1,296
Series A redeemable preferred stock	-	-	-	-	-	-	-	-	-
Total liabilities	271,416	231,919	214,399	205,393	189,594	173,795	173,795	92,003	56,531
Stockholders' equity	25,274	7,684	6,668	2,921	(7,266)	(17,939)	(17,939)	(57,205)	(81,650)
Total liabilities and stockholders' equity	296,690	239,603	221,067	208,314	182,328	155,856	155,856	34,799	(25,118)

Sources: Medivation, Inc. and William Blair & Company, L.L.C.

Table 21
Medivation, Inc.
Statement of Cash Flows
(dollars in thousands)

	2009A	2010A	2011E	2012E	2013E
Net cash from operating activities					
Net income (loss)	(\$54,753)	(\$34,037)	(\$41,036)	(\$44,515)	(\$32,445)
Adjustments					
Stock-based compensation	10,726	13,530	15,724	17,341	18,721
Depreciation and amortization expense	311	465	418	458	508
Deferred taxes	-	-	-	-	-
Accretion of discount on securities	(1,081)	(281)	-	-	-
Change in operating assets and liabilities					
Accounts receivable	(2,968)	(14,698)	6,425	-	(2,000)
Prepaid expenses	(5,450)	(224)	1,276	(1,209)	(1,000)
Other assets	78	(322)	-	-	-
Accounts payable	(2,326)	(1,611)	3,056	-	1,000
Accrued expenses	6,282	9,345	2,802	-	1,500
Other current liabilities	707	4,393	(4,734)	-	-
Other noncurrent liabilities	144	884	(142)	-	-
Deferred collaboration revenue	40,745	(52,508)	(59,106)	(81,792)	(37,972)
Net cash used in operating activities	(7,585)	(75,064)	(75,317)	(110,266)	(53,830)
Cash flows from investing activities					
Purchase of property and equipment	(631)	(197)	26	(80)	(100)
Purchases of restricted cash	(1,500)	1,500	-	-	-
Purchases of available-for-sale securities	(342,437)	(209,888)	(100,000)	-	(17,051)
Maturities of available-for-sale securities	272,000	331,000	150,000	20,000	-
Sales of available-for-sale securities	-	-	-	-	-
Net cash used in (provided by) investing activities	(72,568)	122,415	50,026	19,920	(17,151)
Cash flows from financing activities					
Proceeds from common stock issuance, public offer	62,059	-	-	-	-
Warrant exercise	167	-	-	-	-
Excess tax benefits from stock-based compensation	714	278	-	-	-
Proceeds from common stock issuance, employee	3,222	2,625	4,500	5,250	8,000
Net proceeds from stockholder securities law settlement	-	-	2,959	-	-
Net cash provided by financing activities	66,162	2,903	7,459	5,250	8,000
Cash balance (beginning of period)	71,454	57,463	107,717	89,885	4,788
Difference	(13,991)	50,254	(17,832)	(85,096)	(62,981)
Cash balance (end of period)	57,463	107,717	89,885	4,788	(58,192)
Marketable securities	220,781	100,039	39,978	2,179	-
Cash balance plus marketable securities (end of period)	278,244	207,756	129,863	6,967	(58,192)

Sources: Medivation, Inc. and William Blair & Company, L.L.C.

OncoGenex Pharmaceuticals, Inc.

Novel Technology Against a Novel Target in Prostate Cancer

We are initiating coverage of OncoGenex with an Outperform rating and a 12-month price target of \$21.

OncoGenex's lead asset is custirsen, currently in two Phase III studies in combination with chemotherapy in metastatic castration-resistant prostate cancer (mCRPC). Both studies read out during fourth quarter 2013. Custirsen is an antisense agent targeting clusterin, a cell survival protein that is overexpressed when cells are exposed to stressors such as chemotherapy, conferring resistance. Clusterin is a difficult target for small-molecule or antibody therapeutics, and custirsen is an antisense approach to abolish clusterin mRNA, thereby lowering clusterin protein levels and overcoming resistance to chemotherapy.

We assign a conservative 60% probability of success for custirsen. Among the Phase III agents in development in combination with Taxotere in prostate cancer treatment, custirsen is the only one that has demonstrated an impressive overall survival (OS) benefit in a randomized Phase II study. We believe the chance of success of the Phase III study is higher than other novel mechanisms of action, such as anti-angiogenesis.

Our estimate for peak worldwide sales of custirsen in prostate cancer is \$570 million; revenues in other cancer indications would provide upside. Based on its mechanism of action, custirsen can be used in combination with most chemotherapy agents, leading to much broader utility. A Phase III study in non-small cell lung cancer will be initiated in the near future; however, we do not include indications other than prostate cancer in our model.

Our probability-adjusted NPV analysis suggests a \$21 price target. From \$570 million in worldwide sales for custirsen in prostate cancer, 60% probability of success, 50-50 profit sharing with partner Teva in the United States, and a blended 15% net royalty for sales outside the United States, we derive our \$21 price target. Pipeline programs, such as OGX-427, are upside to our valuation.

OncoGenex is a biopharmaceutical company that employs antisense technology to develop therapeutics for cancer. The lead candidate, custirsen, is in Phase III studies for prostate cancer. OncoGenex is based in Bothell, Washington.

Healthcare | Biotechnology

Stock Rating: **Outperform**
Company Profile: **Aggressive Growth**
Price Target: **\$21**

Symbol: OGXI (NASDAQ)
Price: \$9.99 (52-Wk.: \$9-\$20)
Market Value (mil.): \$97
Fiscal Year End: December
Dividend Yield: None

Estimates	2010A	2011E	2012E
EPS FY	(\$1.79)	(\$2.08)	(\$2.35)
Sales (mil.)	\$13.6	\$6.9	\$7.5

Valuation			
FY P/E	NM	NM	NM

Trading Data	
Shares Outstanding (mil.)	9.73
Float (mil.)	8.94
Average Daily Volume (thous.)	59.9

Financial Data	
Total Debt/Total Capital	19%
Enterprise Value (mil.)	\$29
Price/Book	4.7

Investment Summary

Custirsen Potentiates Chemotherapy and Could Have Broad Utility

Custirsen is a second-generation antisense agent that potently inhibits clusterin expression and has been shown to improve efficacy of chemotherapy in vitro, in vivo, and more recently, in clinical studies. Clusterin is a cell survival protein and is induced by stress, such as chemotherapy, radiotherapy, or hormonal therapy. Overexpression of clusterin leads to resistance to such therapies and limits their efficacy.

Custirsen is being studied in combination with chemotherapy to break through resistance and improve survival and tolerability. The indications being studied are mCRPC and non-small cell lung cancer (NSCLC).

Custirsen Partnerships with Teva and Isis

In December 2009, OncoGenex signed a global development agreement with Teva on custirsen. Under the terms of the agreement, Teva paid OncoGenex \$60 million up front, including a \$10 million equity investment. OncoGenex is eligible to receive up to \$370 million in clinical, regulatory, and sales milestones as well as tiered royalties ranging from the mid-teens to mid-20s. OncoGenex also retains the option to co-promote custirsen in the United States and Canada.

On expense sharing, OncoGenex was to commit \$30 million in development costs; the estimated total cost of the Phase III programs of custirsen is \$170 million. There was a roughly \$20 million commitment remaining at mid-2011.

OncoGenex licensed the antisense technology from Isis Pharmaceuticals. It owes Isis about 5% in royalties on custirsen sales, and Isis also has 30% interest in any non-royalty payments, such as milestones.

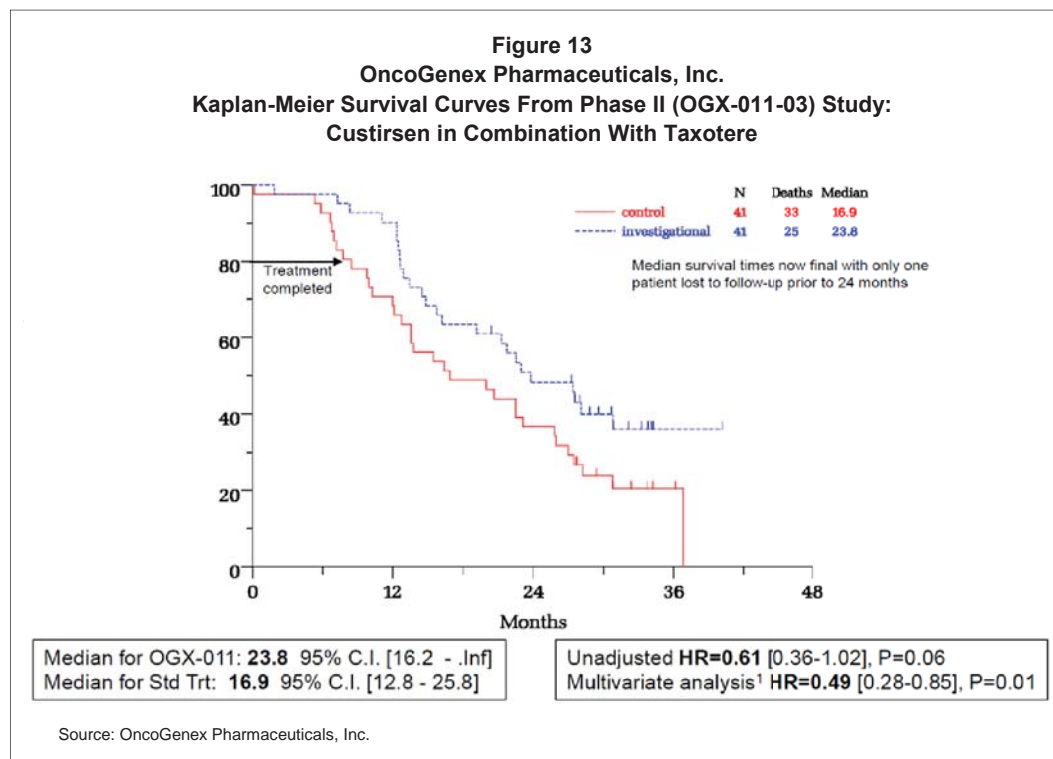
Randomized Phase II Study of Custirsen in Combination with Taxotere Produced Impressive Data

Study design. In September 2005, OncoGenex initiated a randomized Phase II study (OGX-011-03), which randomized 82 patients one-to-one to receive either once-weekly (QW) intravenous custirsen in combination with docetaxel once every three weeks (Q3W), or docetaxel alone. Patients enrolled in the combination arm received three loading doses of custirsen in the first week of treatment. All patients received oral prednisone (5 mg twice daily), part of the docetaxel regimen. Patients continued to receive therapy until disease progression, unacceptable toxicity, or completion of 10 3-week cycles of the assigned regimen. Enrollment was completed in December 2006.

The primary endpoint of the study was the proportion of patients with a confirmed prostate-specific antigen (PSA) response (decline of greater than or equal to 50% from baseline). Additional objectives of the study included the objective response rate (ORR), progression-free survival (PFS), overall survival (OS), changes in serum clusterin, safety, and tolerability. One patient withdrew before starting treatment in the custirsen+docetaxel combo arm, but was included in the final intent-to-treat (ITT) analyses for overall survival. Baseline patient characteristics for the study are summarized in table 5, on page 18.

Custirsen+docetaxel combo demonstrates an impressive 6.9-month improvement in OS over docetaxel alone; PSA response similar, ORR and PFS slightly better. Fifty-eight percent of patients treated in the custirsen+docetaxel combo arm achieved confirmed PSA declines of 50% or greater, compared with 54% of patients treated with docetaxel alone. The ORRs were comparable between the two arms of the study, with five patients (19%) in the custirsen+docetaxel cohort and six patients (25%) in the docetaxel-alone cohort achieving a partial response (PR). Additionally, the combination arm achieved a higher rate of stable disease and a lower rate of disease progression.

The final analysis of the study showed that the combination arm achieved a median OS of 23.8 months compared with 16.9 months with the docetaxel arm, with an unadjusted hazard ratio (HR) of 0.61 ($p=0.06$), as shown in figure 13.



Median progression-free survival (PFS) observed for the custirsen+docetaxel arm was 7.3 months versus 6.1 months for docetaxel alone, resulting in an HR of 0.88. PSA progression-free survival for the combo and docetaxel cohorts was 8.8 and 8.5 months, respectively.

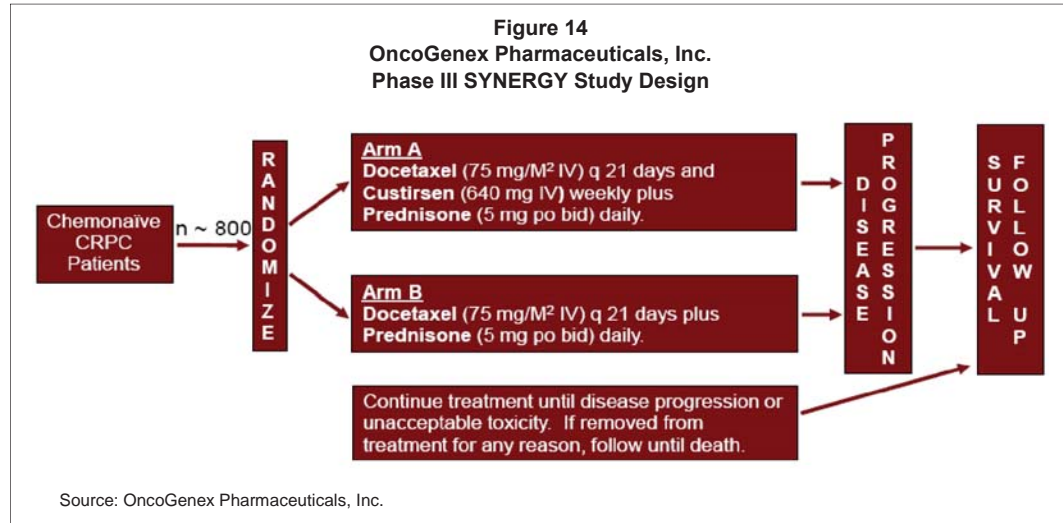
Most common side effects are lymphopenia and cytokine storm. The combination of custirsen+docetaxel was generally safe and well tolerated. The median number of cycles received by patients in the custirsen+docetaxel arm was nine versus seven for patients in the docetaxel-only cohort. Discontinuations because of adverse events were 30% for the combo cohort and 12% for the docetaxel cohort, while discontinuations resulting from disease progression were 18% and 39%, respectively. The most common side effects associated with the treatment of custirsen+docetaxel include lymphopenia, rigor (chills), fever, and elevated creatinine. Chills and fever typically occurred during the loading-dose phase of the custirsen arm (first week of treatment).

Statistically significant declines in serum clusterin (sCLU) levels. A key secondary endpoint met in the study was the median change in baseline sCLU levels. Treatment with the combination of custirsen+docetaxel led to a significant decline in sCLU levels of 13% (day 15, $p=0.05$) and 26% (day 22, $p=0.005$) in cycle 1 of treatment, compared with an increase of 2% and 1%, respectively, with the treatment of docetaxel alone. This pharmacodynamic measurement is supportive evidence that the treatment of custirsen has the intended biological effect on its target clusterin.

SYNERGY: Custirsen in Combination With Taxotere in the Frontline Chemotherapy Setting With Overall Survival as Primary Endpoint

Design. Following the promising results from the Phase II study, OncoGenex and partner Teva Pharmaceuticals initiated the Phase III SYNERGY study in September 2010 (figure 14, on the following page). The multicenter, randomized, global study plans to enroll 800

men with mCRPC seeking first-line chemotherapy treatment with Taxotere. Patients are randomized one-to-one to either the combo of custirsen+docetaxel or docetaxel alone. Similar to the Phase II design, both cohorts will receive daily prednisone.



The primary endpoint of the study is OS, while secondary endpoints include measurements of PFS, PSA response, and safety. Patients will receive the assigned treatment until disease progression, unacceptable toxicity, or the completion of 10 cycles of the regimen. The study is expected to complete accrual by the second half of 2012, and top-line results from the study are expected by year-end 2013.

SYNERGY is being conducted under a Special Protocol Assessment (SPA) process approved by both the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA). Custirsen has received fast-track designation from the FDA for the treatment of metastatic prostate cancer in combination with first-line docetaxel, and importantly, the agency has also guided that an application supported primarily by results from the SYNERGY study alone would be acceptable for submission of custirsen’s regulatory approval.

We assign a 60% probability of success for SYNERGY in our model. Based on the promising randomized Phase II data, we believe it is more likely than not that the Phase III study will be successful, should the design, powering assumptions, and conduct of the study be satisfactory.

SATURN: Custirsen in Combination With Taxotere or Jevtana in Second-Line Chemo Setting With Pain Palliation as Primary Endpoint

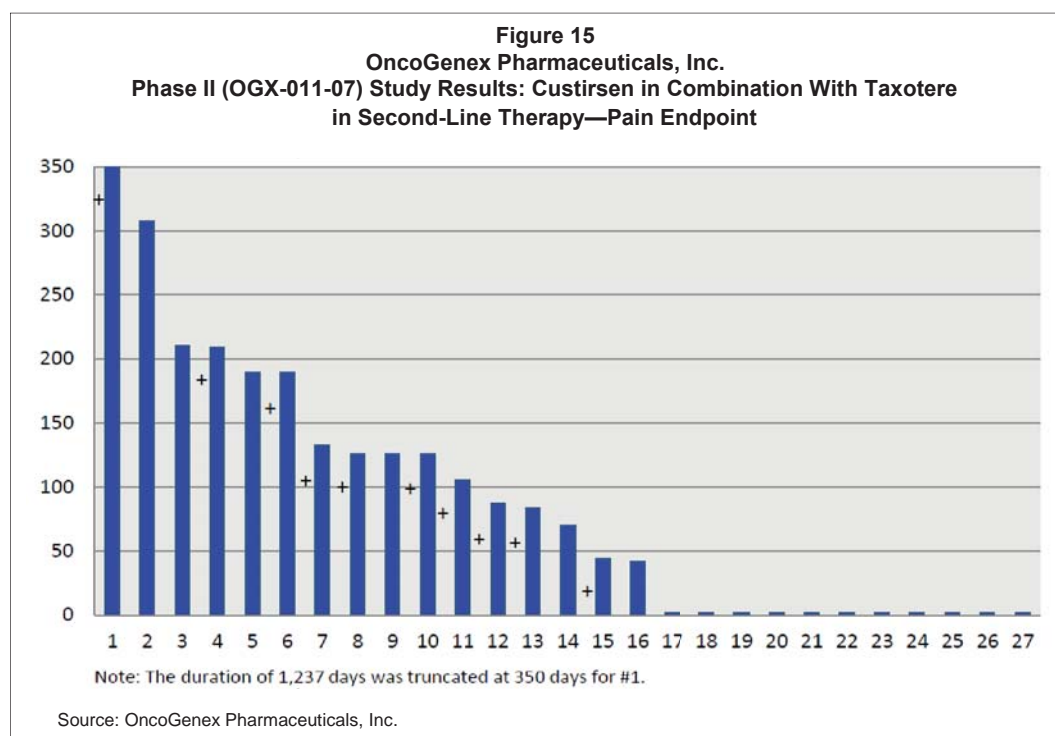
Phase II pain study design. Initiated in 2006, the open-label randomized Phase II study (OGX-011-07) enrolled 42 patients, with mCRPC progressing during or within six months of initial docetaxel therapy. Patients eligible for the study had to have received a minimum of two cycles of docetaxel. Patients were randomized one-to-one to receive either custirsen+docetaxel (640 mg iv Q1W and 75 mg/m² iv Q3W, respectively) or custirsen+mitoxantrone (640 mg iv Q1W and 12 mg/m² iv Q1W, respectively); both cohorts received daily prednisone. Following the randomization segment of the study, an additional 25 mCRPC patients were recruited to the custirsen+docetaxel cohort.

The primary endpoint of the study was to evaluate the safety and tolerability of custirsen in combination with second-line chemotherapy. Key secondary outcomes included PSA response and time-to-pain progression.

Phase II study in mCRPC patients with second-line chemotherapy demonstrated promising pain palliation; safety profile adequate. Sixty percent, or 27 of the 45 patients in the custirsen+docetaxel arm, entered the study either taking opioid analgesics or with prostate cancer–related pain. Pain palliation, defined as a decrease of greater than or equal to two points on an 11-point scale or a decrease in opioid use maintained for a minimum of three weeks, was observed in 16 of 27 patients (59%), as shown in figure 15. Importantly, 81% of patients experiencing pain palliation achieved a durable response, defined as pain palliation for three months or more.

As a reference, the Jevtana (cabazitaxel) Phase III TROPIC study demonstrated pain responses in 9.2% and 7.7% of patients with baseline pain in the cabazitaxel and mitoxantrone arms, respectively. In the Zytiga post-Taxotere mCRPC study COU-AA-301, pain palliation was 44% for Zytiga versus 27% for placebo in patients with baseline pain score of 4 or more.

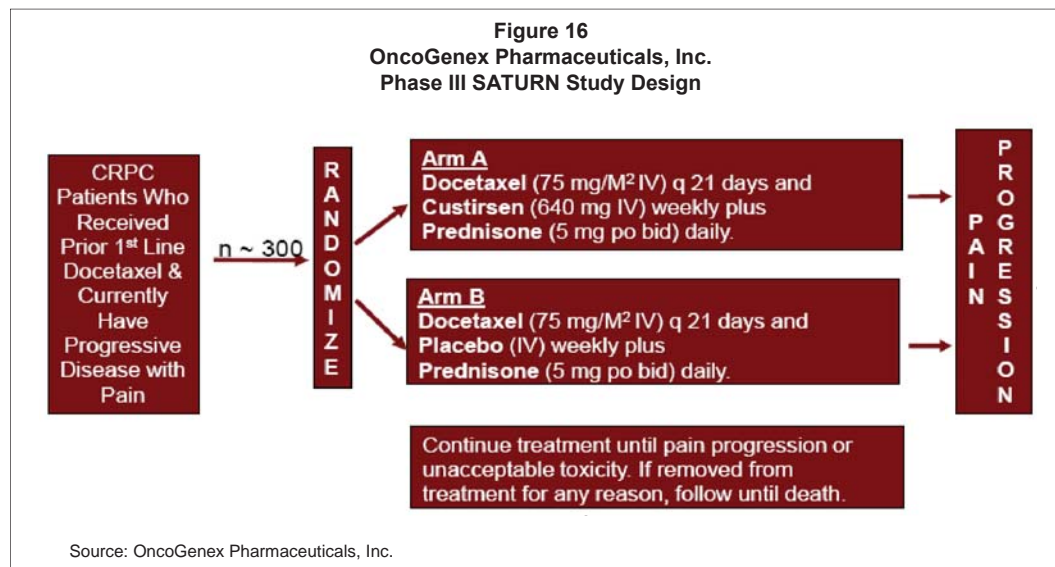
Results from the study also demonstrated that the combination of custirsen with either chemotherapy was both safe and well tolerated in the second-line setting. Patients received a median of eight cycles and six cycles of custirsen+docetaxel and custirsen+ mitoxantrone, respectively. Grade 3 or 4 adverse events in the study included fatigue, lymphopenia, and neutropenia.



SATURN is a Phase III study seeking the pain palliation endpoint. In June 2010, OncoGenex and partner Teva initiated the Phase III SATURN study in mCRPC patients that had progressed after first-line docetaxel therapy. The placebo-controlled study will enroll and randomize roughly 300 patients, with concurrent prostate cancer–related pain, to receive either custirsen or placebo in combination with docetaxel (and prednisone) as second-line chemotherapy. With the approval of Jevtana (cabazitaxel) for second-line mCRPC in June 2010, the company submitted a revised SPA to the FDA for the study earlier this year to amend the protocol to allow patients to receive either docetaxel retreatment or cabazitaxel as second-line chemotherapy.

The primary endpoint of the study is to evaluate the proportion of patients who experience durable pain palliation (greater than 12 weeks) with treatment of custirsen versus placebo. Secondary endpoints include time-to-pain progression (TTPP) and safety. Because of

restrictive enrollment criteria regarding docetaxel retreatment and pain, the expected timing of top-line results for the primary endpoint (pain palliation) has been revised; results are now expected to be reported by year-end 2013 (previously guided for second quarter 2013). The Phase III SATURN design is summarized in figure 16.



Custirsen in Combination With Platinum-Based Doublet in First-Line Non-Small Cell Lung Cancer (NSCLC)

Single-arm Phase II study results encouraging. Initiated in 2004, the open-label, single-arm Phase II study (OGX-011-05) enrolled 81 chemo-naïve stage III/IV NSCLC patients to receive the combination of custirsen with either gemcitabine+cisplatin (GemCis) or gemcitabine+carboplatin (GemCarbo). The primary objective of the study was to determine the objective response rate (ORR) of the triple combination, while secondary outcomes included progression-free survival, overall survival, and the pharmacokinetic profile of custirsen in combination with GemCis or GemCarbo. (See figure 17, opposite.)

Median overall survival for the study was 14.1 months compared with historical controls of 8.0 to 10.8 months. The median PFS was 4.6 months. In addition, 54% and 30% of patients survived more than one year and two years, respectively; this compares to combinations using therapies such as cisplatin, carboplatin, paclitaxel, docetaxel, vinorelbine, gemcitabine, and pemetrexed (Alimta), which have demonstrated one-year survival rates of 30% to 40%.

Initiation of planned Phase III study now expected to begin in 2012. OncoGenex and Teva previously planned to initiate the Phase III NSCLC study this year; however, the study has been delayed until satisfactory completion of the ongoing drug-drug interaction (DDI) studies between custirsen and paclitaxel.

The proposed Phase III NSCLC study design, as shown in figure 18, opposite, will enroll and randomize roughly 950 chemo-naïve stage IV patients into the triple combination of custirsen+paclitaxel+carboplatin or the doublet paclitaxel+carboplatin. The proposed primary endpoint of the study is overall survival, while the key secondary endpoint is progression-free survival at 12 weeks. One efficacy interim analysis and two futility interim analyses are also included in the design.

OncoGenex's Second Novel Clinical Candidate, OGX-427, Targets Chaperone Heat Shock Protein 27 (Hsp27)

OGX-427 is a second-generation antisense agent that inhibits production of the cell survival protein Hsp27, resulting in apoptosis and cell growth inhibition. Similar to custirsen, OGX-427 can also act as a chemosensitizer. Increased expression of Hsp27 has been associated with metastases, poor prognosis, and resistance to radiation and has been implicated in castration-resistant progression of prostate cancer. OGX-427 is a second candidate from the company's collaboration and license agreement with Isis.

OGX-427 is being evaluated in a randomized Phase II study as a monotherapy treatment for mCRPC and in an ongoing Phase I study for superficial bladder cancer. Additionally, OncoGenex plans to initiate a Phase II study evaluating OGX-427 in frontline bladder cancer by year-end 2011.

Ongoing OGX-427 Phase II Study in mCRPC. In September 2010, OncoGenex initiated a Phase II study evaluating monotherapy OGX-427 in 72 chemo-naïve patients with minimally symptomatic or asymptomatic advanced prostate cancer. The primary efficacy endpoint of the study is the proportion of patients without disease progression at 12 weeks post-study treatment, while secondary endpoints include PSA response and time-to-PSA progression (TTPP). Data from the Phase II study are expected by year-end 2012.

Risks to Our Outperform Rating

Risks to our Outperform rating and attainment of our price target include failure to meet efficacy endpoints for the Phase III programs of custirsen, unforeseen safety issues in longer-term studies, setbacks in clinical and business development, and financing risk.

Valuation

In building the probability-adjusted net present value (NPV) model, we estimate the peak sales of a particular drug candidate, its probability of advancing to the next stage of development and eventually reaching the market, and the company's share of revenue and expenses, depending on the commercialization plan and/or structure of any partnerships. We then calculate the cash flows after adjusting all revenues and expenses with respective cumulative probabilities for each stage. The cash flows are discounted back using an industry-specific weighted average cost of capital of 12% to arrive at a probability-adjusted NPV for each drug candidate. Once we determine the NPV for each candidate, we then add net cash and other costs, which include expenses not directly associated with the development of the clinical candidates, to arrive at a fair value estimate for the stock.

With \$570 million worldwide sales for custirsen in prostate cancer, 60% probability of success, 50-50 profit sharing with partner Teva in the United States, and blended 15% net royalty for sales outside the United States, we derive our \$21 price target.

Table 22
OncoGenex Pharmaceuticals, Inc.
Sum-of-the-Parts Fair Value
(dollars in thousands)

Drug	Peak Sales	Stage of Development	Estimated Launch Date	Probability of Commercialization	Percentage of Sales to Company	Probability-Adjusted NPV	Value Per Share	Percentage of Fair Value
Custirsen in CRPC—United States	\$339,676	Phase III	Q3:2014	60%	50:50 profit share with Teva	\$143,169	\$14.64	69.7%
Custirsen in CRPC—European Union	\$229,427	Phase III	Q1:2015	60%	15%	\$44,404	\$4.54	21.6%
Subtotal						\$187,574	\$19.18	91.3%
Net Cash at Year End 2012						\$31,343	\$3.21	15.3%
Net Present Value of additional Gain (Loss)*						(\$13,393)	(\$1.37)	(6.5%)
Sum-of-the-Parts Fair Value						\$205,524	\$21.02	100.0%

* Includes costs not directly related to programs above

Sources: Company reports and William Blair & Company, L.L.C. estimates

Management Team

Table 23
OncoGenex Pharmaceuticals, Inc.
Brief Biographies of Management Team

Management	Position	Previous Experience
Scott Cormack	President and Chief Executive Officer	Interim President and Chief Executive Officer, Salpep Biotechnology Inc.; Vice President, Milestone Medica Corporation; Chief Operating Officer, NeuroSpheres Ltd
Michelle Burris	Executive Vice President—Operations and Chief Financial Officer	Senior Vice President and Chief Operating Officer, Trubion Pharmaceuticals, Inc.; Senior Vice President and Chief Financial Officer, Dendreon Corporation; Senior Vice President and Chief Financial Officer, Corixa Corporation
Cindy Jacobs, Ph.D., M.D.	Executive Vice President and Chief Medical Officer	Senior Vice President—Clinical Development and Chief Medical Officer, Corixa Corporation; Vice President—Clinical Research, Cytran Inc.
Monica Krieger, Ph.D.	Vice President—Regulatory Affairs	Vice President—Regulatory Affairs, Corixa Corporation; Vice President—Regulatory, Clinical and Quality Assurance, Genetic Systems Corporation
Cameron Lawrence	Principal Accounting Officer	Director—Financial Reporting, OncoGenex Pharmaceuticals, Inc.; Manager—Audit and Assurance Group, PricewaterhouseCoopers LLP
Martin Gleave, M.D.	Chief Scientific Advisor	Chief Scientific Officer, OncoGenex Pharmaceuticals; Professor and Research Director, Department of Urologic Sciences, University of British Columbia; Director—Clinical Research of Prostate Center, Vancouver General Hospital

Source: OncoGenex Pharmaceuticals, Inc.

Upcoming Catalysts

The major catalysts for custirsen are the Phase III data releases, which are not due until fourth quarter 2013. In the next year or so, clinical development news on OGX-427 will serve as catalysts for the stock.

Table 24
OncoGenex Pharmaceuticals, Inc.
Clinical Development Timeline/Milestones

Drug	Custirsen (OGX-011)	Custirsen (OGX-011)	OGX-427	OGX-427
Indication	Prostate cancer	Non-small cell lung cancer	Prostate cancer	Bladder cancer
Class	Antisense against clusterin	Antisense against clusterin	Antisense against Hsp27	Antisense against Hsp27
Partner	Teva	Teva		
1Q 2010				
2Q 2010	Initiated Phase III SATURN study (second line after Taxotere, pain endpoint, n=300)			
3Q 2010	Initiated Phase III SYNERGY study (in combo with Taxotere, n=800)			
4Q 2010			Initiated Phase II (n=72), monotherapy in pre-chemo asymptomatic CRPC	
1Q 2011				
2Q 2011				
3Q 2011				
4Q 2011		Phase III to be initiated after DDI studies satisfactory (n=950)		Initiate Phase II study (with frontline chemo)
1Q 2012			Potential interim Phase II results	Potential interim Phase II results (superficial bladder)
2Q 2012				
3Q 2012				
4Q 2012			Phase II results (Primary endpoint: percent of patients without disease progression)	Phase II results for superficial bladder (Primary endpoint: percent of patients without disease progression)
1Q 2013				
2Q 2013				
3Q 2013				
4Q 2013	Phase III SATURN top-line results; Phase III SYNERGY top-line results			

P/R: PEG-Interferon + Ribavirin

Brown highlight: Events likely to affect the stock price

Sources: Company reports and William Blair & Company, L.L.C. estimates

Additional information is available upon request.

This report is available in electronic form to registered users via R*Docs™ at www.rdocs.com or www.williamblair.com.

Please contact us at (800) 621-0687 or consult http://www.williamblair.com/pages/eqresearch_coverage.asp for all disclosures.

DJIA: 11,246.73
 S&P 500: 1,188.68
 NASDAQ: 2,572.55

Table 25
OncoGenex Pharmaceuticals, Inc.
Income Statement
(dollars in thousands)

	2009A	2010A	2011E					2012E	2013E
			Q1A	Q2A	Q3E	Q4E	FY:11E		
Revenues									
OGX-011 U.S. revenue	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
OGX-011 ex-U.S. royalties	-	-	-	-	-	-	-	-	-
Collaboration revenue	25,539	13,616	1,199	1,887	1,887	1,887	6,860	7,548	7,548
Total Revenues	25,539	13,616	1,199	1,887	1,887	1,887	6,860	7,548	7,548
Expenses									
COGS	-	-	-	-	-	-	-	-	-
R&D expense	20,209	18,483	4,853	5,409	5,679	5,793	21,734	24,354	25,716
SG&A expense	3,961	5,840	1,571	1,471	1,486	1,501	6,028	6,154	6,404
Restructuring expense	3,951	4,038	-	-	-	-	-	-	-
Total Operating Expenses	28,121	28,361	6,424	6,880	7,165	7,294	27,763	30,508	32,119
Operating income	(2,582)	(14,745)	(5,225)	(4,993)	(5,278)	(5,407)	(20,903)	(22,960)	(24,571)
Interest income/(expense), net	47	86	56	63	38	34	191	101	37
Other income/(expense), net	70	6	(4)	87	-	-	83	-	-
Warrant issuance costs	-	(1,027)	2,128	(1,687)	-	-	441	-	-
Gain (loss) on warrants	-	96	-	-	-	-	-	-	-
Pretax income/(loss)	(2,465)	(15,584)	(3,045)	(6,530)	(5,240)	(5,372)	(20,188)	(22,859)	(24,535)
Provision for income taxes/(income)	3,011	(3,000)	-	-	-	-	-	-	-
Loss before extraordinary gain	(5,476)	(12,584)	(3,045)	(6,530)	(5,240)	(5,372)	(20,188)	(22,859)	(24,535)
Extraordinary gain	-	-	-	-	-	-	-	-	-
Redeemable convertible preferred share accretion	-	-	-	-	-	-	-	-	-
Net Income/(Loss)	(\$5,476)	(\$12,584)	(\$3,045)	(\$6,530)	(\$5,240)	(\$5,372)	(\$20,188)	(\$22,859)	(\$24,535)
GAAP EPS	(\$0.95)	(\$1.79)	(\$0.31)	(\$0.67)	(\$0.54)	(\$0.55)	(\$2.08)	(\$2.35)	(\$2.51)
Weighted average shares outstanding, diluted	5,767	7,031	9,713	9,718	9,723	9,728	9,721	9,741	9,767

Sources: OncoGenex Pharmaceuticals, Inc. and William Blair & Company L.L.C. estimates

Table 26
OncoGenex Pharmaceuticals, Inc.
Balance Sheet
(dollars in thousands)

	2009A	2010A	2011E					2012E	2013E
			Q1A	Q2A	Q3E	Q4E	FY:11E		
Current assets									
Total cash, cash equivalents, short-term investments	\$64,568	\$85,107	\$81,098	\$75,412	\$68,523	\$61,373	\$61,373	\$31,343	(\$1,916)
Restricted cash	-	502	502	502	502	502	502	502	502
Accounts receivable	3,109	1,224	1,348	1,498	1,510	1,610	1,610	1,510	1,547
Inventories	-	-	-	-	-	-	-	-	-
Prepaid expense and other	722	2,485	968	1,397	1,397	1,397	1,397	1,597	1,797
Total current assets	68,399	89,318	83,916	78,809	71,932	64,882	64,882	34,952	1,930
Property, plant and equipment, net	72	87	171	207	227	247	247	327	427
Other noncurrent assets	509	513	510	509	509	509	509	509	509
Total assets	68,980	89,918	84,597	79,525	72,668	65,638	65,638	35,788	2,866
Current liabilities									
Accounts payable and accrued liabilities	14,453	893	1,166	1,643	1,863	2,042	2,042	2,350	2,445
Deferred collaboration revenue	10,000	10,000	10,000	10,000	10,000	10,000	10,000	8,544	996
Current portion of long-term obligations	1,328	1,314	1,305	1,384	1,384	1,384	1,384	1,384	-
Warrant liability	-	15,269	13,141	14,828	14,828	14,828	14,828	14,828	14,828
Total current liabilities	25,781	27,476	25,612	27,855	28,075	28,254	28,254	27,106	18,269
Deferred revenue, net of current	16,528	11,622	11,040	9,866	7,979	6,092	6,092	-	-
Long-term obligations, less current portion	3,712	6,695	6,447	6,606	6,606	6,606	6,606	6,606	6,606
Total liabilities	46,021	45,793	43,099	44,327	42,660	40,952	40,952	33,712	24,875
Stockholders' equity	22,959	44,125	41,498	35,198	30,008	24,685	24,685	2,076	(22,009)
Total liabilities and stockholders' equity	68,980	89,918	84,597	79,525	72,668	65,638	65,638	35,788	2,866

Sources: OncoGenex Pharmaceuticals, Inc. and William Blair & Company, L.L.C. estimates

Table 27
OncoGenex Pharmaceuticals, Inc.
Statement of Cash Flows
(dollars in thousands)

	2009A	2010A	2011E	2012E	2013E
Net cash from operating activities					
Net income (loss)	(\$5,476)	(\$12,584)	(\$20,188)	(\$22,859)	(\$24,535)
Adjustments					
Extraordinary loss	-	-	-	-	-
Warrant issuance costs	-	1,027	-	-	-
Change in value of warrants	-	(96)	(500)	-	-
Stock-based compensation	380	642	972	1,068	1,124
Depreciation & amortization expense	50	52	62	82	107
Accrued interest on convertible debenture	-	-	-	-	-
Restructuring expense	3,951	4,038	-	-	-
Change in operating assets and liabilities					
Accounts receivable	(2,955)	1,885	(386)	100	(38)
Investment tax credit recoverable	1,090	-	-	-	-
Prepaid expenses	(136)	(1,763)	1,088	(200)	(200)
Restricted cash	-	(502)	-	-	-
Other assets	(12)	(4)	-	-	-
Accounts payable and accrued liabilities	12,200	(13,560)	1,149	307	95
Lease obligation	(741)	(1,069)	(40)	-	-
Taxes payable on preferred shares	-	-	-	-	-
Deferred collaboration revenue	26,527	(4,906)	(5,460)	(6,092)	(1,384)
Net cash used in operating activities	34,878	(26,840)	(23,303)	(27,594)	(24,830)
Cash flows from investing activities					
Purchase of property and equipment	(15)	(68)	(160)	(80)	(100)
Purchases of available-for-sale securities	(4,036)	(93,018)	(100,000)	-	(282)
Proceeds of available-for-sale securities	6,280	33,960	150,000	-	-
Cash received on reverse takeover of Sonus	-	-	-	-	-
Transaction fees on reverse takeover of Sonus	-	-	-	-	-
Net cash used in (provided by) investing activities	2,229	(59,126)	49,840	(80)	(382)
Cash flows from financing activities					
Cash paid on fractional shares eliminated on reverse share split	-	-	-	-	-
Issuance of common shares, net of share issue cost	17,206	32,319	-	-	-
Issuance of warrants, net of warrant issuance cost	-	14,338	-	-	-
Proceeds from common stock issuance, employee	141	824	200	250	450
Net cash provided by financing activities	17,347	47,481	200	250	450
Effect of exchange rate changes on cash	(21)	(33)	-	-	-
Cash balance (beginning of period)	7,618	62,051	23,533	50,270	22,846
Difference	54,433	(38,518)	26,737	(27,424)	(24,762)
Cash balance (end of period)	62,051	23,533	50,270	22,846	(1,916)
Marketable securities	2,517	61,574	11,103	8,497	-
Cash balance plus marketable securities (end of period)	64,568	85,107	61,373	31,343	(1,916)

Sources: OncoGenex Pharmaceuticals, Inc. and William Blair & Company L.L.C. estimates

The prices of the common stock of other public companies mentioned in this report follow:

Astellas Pharma, Inc.	\$38.10
AstraZeneca plc	\$44.18
BioSante Pharmaceuticals, Inc.	\$2.80
Bristol-Myers Squibb Company	\$29.63
Celgene Corporation (Outperform)	\$60.23
Exelixis Inc. (Outperform)	\$7.28
Isis Pharmaceuticals, Inc.	\$7.14
Johnson & Johnson	\$63.73
Merck KGaA	\$56.95
Pfizer Inc.	\$18.41
Regeneron Pharmaceuticals, Inc.	\$63.51
Sanofi	\$32.86
Teva Pharmaceutical Industries Limited	\$38.33

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Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	59%	Outperform (Buy)	8%
Market Perform (Hold)	31%	Market Perform (Hold)	2%
Underperform (Sell)	1%	Underperform (Sell)	0%

* Percentage of companies in each rating category that are investment banking clients, defined as companies for which William Blair has received compensation for investment banking services within the past 12 months.

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