March 12, 2012

AVEO Pharmaceuticals

(AVEO-NASDAQ)

Stock Rating: **Market Perform**
Industry Rating: **Outperform**

Biotechnology

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Initiating Coverage With MARKET PERFORM Rating

Investment Thesis

We are initiating coverage of AVEO Pharmaceuticals with a **MARKET PERFORM** rating and $13 price target. We believe the shares are fully valued for tivozanib opportunity in renal cell carcinoma (RCC) and that upside potential from additional indications will be difficult to realize given narrow activity of the drug. While TIVO-1 data suggest superior progression free survival (PFS) and potentially better tolerability than approved brand Nexavar in RCC, expert feedback suggests that magnitude of benefit is insufficient to supplant frontline drugs and that favorable tolerability best positions tivozanib as a preferred salvage agent in later rounds of therapy. As a treatment alternative sequenced ahead of Nexavar in RCC, we estimate peak tivozanib sales of $150M in the US and insufficient to support profitability. With highly selective anti-VEGF activity, we see less opportunity for tivozanib to succeed outside of RCC, where other less selective VEGF tyrosine kinase inhibitors may benefit from broader effects on KRAS, BRAF, and other key cancer signaling pathways. In particular, with next focus on metastatic colorectal cancer (mCRC), we see a difficult path for tivozanib in a space crowded by frontline Avastin, second-line Erbitux and Vectibix, and potential approval of second-line ZALTRAP and third-line regorafenib.

Forecasts

Our 2012 forecast is for a loss per share of $3.02.

Valuation

Our $13 price target is based on 25x 2017E EPS of $1.00 discounted 20%.

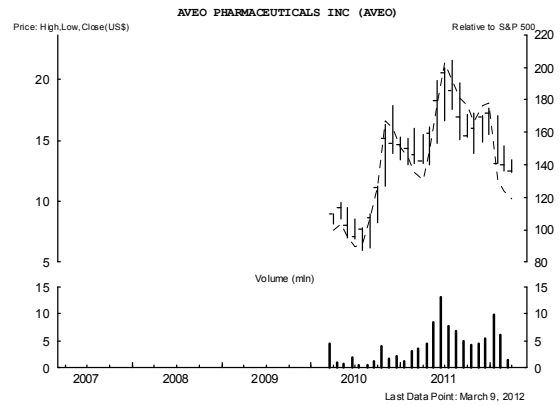
Recommendation

We rate AVEO stock **MARKET PERFORM**.

Securities Info

Price (9-Mar)	**$12.52**	**Target Price**	**$13**
52-Wk High/Low	$22/$12	Dividend	--
Mkt Cap (mm)	$1,190	Yield	--
Shs O/S (mm, BASIC)	95.1	Float O/S (mm)	94.1
Options O/S (mm)	na	ADVol (30-day, 000s)	310

Price Performance



Valuation/Financial Data

(FY-Dec.)	2010A	2011A	2012E	2013E
EPS GAAP	-$2.30	$0.74	-$3.02	-$2.10
P/E			nm	nm
First Call Cons.				
FCF	-$4.97	$0.66	-$3.08	-$2.28
P/FCF			nm	nm
EBITDA ($mm)	-$56	$34	-$128	-$100
EV/EBITDA			nm	nm
Rev. ($mm)	$45	$165	$30	$69
EV/Rev			32.8x	14.2x

Quarterly EPS	**1Q**	**2Q**	**3Q**	**4Q**
2011A	$2.28	-$0.16	-$0.55	-$0.58
2012E	-$0.76	-$0.87	-$0.52	-$0.87

Balance Sheet Data (31-Dec)			
Net Debt ($mm)	-$206	TotalDebt/EBITDA	nm
Total Debt ($mm)	$16	EBITDA/IntExp	na
Net Debt/Cap.	nm	Price/Book	2.4x

Notes: All values in US$.

Source: BMO Capital Markets estimates, Bloomberg, FactSet, Global Insight, Reuters, and Thomson Financial.

Investment Thesis

AVEO has established tivozanib as a highly selective small-molecule VEGF inhibitor with favorable safety and tolerability compared to approved tyrosine kinase inhibitors (TKIs) like Nexavar, Sutent, Inlyta and Votrient. While efficacy appears favorable compared with Onyx's Nexavar, this agent is typically sequenced later in the treatment paradigm for advanced renal cell cancer (RCC) patients, and relative efficacy of tivozanib compared to more potent TKIs like Sutent and Inlyta is less clear.

We believe that both the safety and efficacy profile of tivozanib and relative efficacy comparison to Nexavar is more apt to position the drug as a preferred salvage agent, sequenced ahead of Nexavar, in sicker patients unlikely to tolerate more potent TKIs. In the absence of a head-to-head comparison to Sutent, Avastin, or Votrient, agents with category 1 evidence for frontline use, we believe that it will be difficult for tivozanib to supplant these agents. Indeed, with a clear bias to use more potent agents earlier, when patients can tolerate them, we believe that tivozanib is best sequenced after Sutent, Votrient, Avastin, as well as other second-line agents, and perhaps even after Nexavar.

While Onyx has not broken out Nexavar sales in RCC from that in hepatocellular carcinoma (HCC), we believe that a decline in market share and sales have occurred since sales levels were last reported at roughly $280M, and would estimate global Nexavar sales of ~$200M, with less than $100M in US sales. Assuming that tivozanib is consistently sequenced ahead of Nexavar, as opposed to afterwards where its superior tolerability may be better leveraged, we would estimate a US sales opportunity of no more than $150M, assuming that dosing duration is 50% longer.

We do not believe that AVEO can achieve sustainable profitability with royalties from RCC alone, and expect significant investment in broader indications for tivozanib. We have concerns, however, that the activity of tivozanib may be too narrow to expand use beyond those indications already dominated by Avastin and being followed on by ZALTRAP or the many indications where selective VEGF inhibition has failed. We would note that success of Nexavar in HCC, and activity in NSCLC in particular, may be driven more by KRAS and BRAF activity than anti-VEGF effects, and that regorafenib activity in third line mCRC may also be a function of activity beyond VEGF inhibition. Metastatic colorectal cancer appears to be a particularly crowded area in which to develop tivozanib following success of Avastin, Zaltrap, and regorafenib in the first, second, and third line setting, respectively.

In hepatocellular carcinoma (HCC), where Onyx derives most sales for Nexavar we would note that several VEGF-multikinase inhibitors have already failed, and we would highlight Genentech’s decision to pursue the combination of its anti-VEGF antibody Avastin with EGFR TKI Tarceva in patients with advanced HCC, over treatment with pure VEGF inhibition with Avastin alone, as further evidence of the potential limitations of a highly selective VEGF approach. To that end, we believe that broadening of the tivozanib opportunity beyond RCC will require combination trials with other molecularly targeted agents, and to date would note only 1 phase 1b study of tivozanib + mTOR inhibitor temsirolimus.

Background

AVEO is a development-stage biotechnology company that since inception in 2001 has focused on cancer drug development. AVEO's most advanced asset is tivozanib, an oral small molecule inhibitor of vascular endothelial growth factor receptors (VEGFRs). The compound was not developed internally but rather AVEO licensed ex-Asian rights to tivozanib from Kyowa Hakko Kirin. Subsequently in February 2011, AVEO entered into a co-development and co-commercialization relationship with Astellas for tivozanib. In 1Q12, AVEO reported positive data from an active controlled phase 3 trial of tivozanib in renal cell carcinoma (RCC). An NDA is planned for 3Q12 with a European filing to follow shortly thereafter. AVEO's second most advanced product is an antibody to the hepatocyte growth factor (HGF) receptor, ficlatuzumab (AV-299), which is currently in phase 2 testing. AVEO's third development program is AV-203, an antibody targeting the erbB3 receptor partnered with Biogen Idec.

Not surprisingly most focus is on the NDA and MAA filings for tivozanib for advanced renal cell carcinoma (RCC) and commercial opportunity relative to other VEGF-multikinase inhibitors as well as other molecularly targeted drugs. Secondary focus is on label expansion opportunities for tivozanib beyond RCC, and particularly on randomized phase 2 data comparing FOLFOX + tivozanib vs. FOLFOX alone in patients with metastatic colorectal cancer (mCRC), with data currently expected in 2014. Review of the AVEO pipeline beyond tivozanib reveals a program for anti-HGF antibody ficlatuzumab in patients with squamous cell carcinoma of the head and neck (SCCHN), with phase 2 data expected in 2H12. Finally, earlier-stage efforts are focused on as pre-clinical program partnered with Biogen Idec targeting erbB3 and with an IND filing expected in 2012.

Exhibit 1: AVEO Pipeline- Status and Milestones

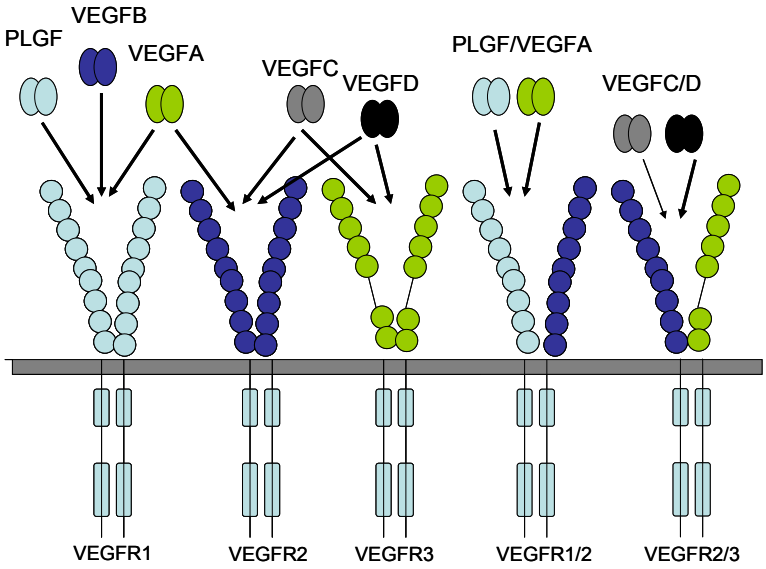
Product	Status	Milestone
Tivozanib - VEGFR Metastatic RCC 1st line CRC	 Phase 3 Phase 2	 NDA 3Q12 Data 4Q14
Ficlatuzumab - HGF IV – H&N	Phase 2	Data 2H12
AV-203- erbB3	Pre-IND	IND 1H12

Sources: Company Documents and BMO Capital Markets estimates.

Tivozanib – VEGF Selective Tyrosine Kinase Inhibitor

Tivozanib is an inhibitor of vascular endothelial growth receptors, VEGFR1, VEGFR2, and VEGFR3. As depicted below, the VEGF receptors can form homodimers or heterodimers and transmit signals from 4 VEGF ligands as well as from placental growth factor (PLGF). As an inhibitor of all three VEGF receptors, tivozanib can theoretically neutralize all VEGF receptor activity.

Exhibit 2: Schematic of VEGF Ligands and Receptors



Source BMO Capital Markets.

Tivozanib is a very potent inhibitor of VEGF receptors 1-3 (with IC50's of 0.21, 0.16 & 0.24nM respectively), and this suggests that the desired degree of VEGF receptor inhibition can be achieved at a lower dose of tivozanib compared to less specific inhibitors. An important theoretical benefit for lowering the tivozanib dose is that off-target effects and toxicities can be minimized. Accordingly, AVEO has highlighted what it believes to be a best-in-class safety profile with tivozanib. The tivozanib dose used in the phase 3 renal cell carcinoma (RCC) trial was 1.5mg/day, more than three-fold lower than the next most potent VEGF receptor inhibitor, Pfizer's Inlyta. The table in Exhibit 2 provides a summary of the specific activity of tivozanib versus approved tyrosine kinase inhibitors (TKIs) for RCC.

Exhibit 3: Specific Activity of VEGFR Inhibitors

	Daily Dose	VEGFR1	VEGFR2	VEGFR3	c-kit	vs VEGFR	PDGFR	vs VEGFR
Tivozanib	1.5mg	0.21	0.16	0.24	1.63	8.0	1.7	8.4
Inlyta	10mg	1.2	0.25	0.29	1.6	2.8	1.7	2.9
Sutent	50mg		10	17	10	0.7	8	0.6
Votrient	800mg	10	30	47	74	2.6	80	2.8
Nexavar	800mg		90	20	68	1.2	80	1.5

Sources: AVEO and BMO Capital Markets.

Thus the selectivity of tivozanib for VEGFR over c-kit is 8-fold greater, over PDGFR 8.4-fold greater, and over FGFR1 422-fold greater. AVEO has suggested, and data seem to bear out so far that this selectivity advantage will manifest itself as a better-tolerated drug than competitors. Thus in an earlier phase 2 RCC trial 15% of patients required tivozanib dose reduction, or interruption compared to 24% to 65% of patients receiving one of the approved agents for RCC.

TIVO-1 Phase 3 – Full Data Expected at ASCO

Based on phase 2 data suggesting a more robust benefit for tivozanib in nephrectomized patients with clear cell disease, AVEO initiated a 517-patient phase 3 trial, TIVO-1, comparing tivozanib three-weeks-on and one-week-off vs. Onyx's approved VEGF-multikinase inhibitor Nexavar. The half-life of tivozanib has been estimated to be ~five days and thus a high degree of VEGFR inhibition would be expected during the one-week-off period. Eligible patients in TIVO-1 were either treatment naïve or previously treated with a non-VEGF targeting systemic therapy. In January 2012, AVEO announced that based on blinded independent review, tivozanib increased progression free survival (PFS) by 2.8 months to 11.9 months compared with Nexavar at 9.1 months. In the previously untreated cohort, that comprised roughly 70% of the study population, PFS was 12.7 months with tivozanib. Tivozanib safety and tolerability were reported to be consistent with phase 2 experience where hypertension was the most commonly observed adverse event (AE). Full data from TIVO-1 are expected to be presented at the ASCO annual meeting in June 2012 with US and EU regulatory filings expected in 2H12. AVEO does not expect priority review and thus a 10-month review clock is expected.

The choice of Nexavar as a comparator in TIVO-1 was supported by FDA, which indicated that AVEO needed to compare tivozanib with an active agent in the front-line setting and that Nexavar was a suitable choice. In our view, Nexavar was chosen as presenting a lower hurdle for superiority as compared with more active frontline agents, such as like Sutent based on historical data.

Tivozanib Phase 2 Randomized Discontinuation Study

Tivozanib was previously evaluated in renal cell carcinoma (RCC) patients using a phase 2 randomized discontinuation trial design. Tivozanib was dosed at 1.5mg/day in a 3 week-on-1-week-off schema. Eligible patients in the study were naïve to VEGF-targeted therapy and received 16 weeks of tivozanib therapy before being re-staged. Patients with a 25% or greater reduction in tumor size received an additional 12 weeks of open label tivozanib, while those

with a 25% or greater increase in tumor size came off study. Patients with stable disease were randomized to receive 12 weeks of tivozanib vs. placebo during the randomized discontinuation phase of the study. The trial enrolled 272 patients who received a median of 8.5 months of therapy (up to 24.5 months). The table below in Exhibit 4 summarizes key characteristics of patients enrolled in the phase 2 randomized discontinuation trial.

Exhibit 4: Baseline Characteristics of Renal Cell Cancer Patients in the Phase 2 Tivozanib Trial

Baseline Demographic	Percent
Clear cell histology	83%
Prior Therapies	
0	54%
1	28%
≥2	19%
MSKCC Risk	
Favorable	29.8%
Intermediate	57.4%
Poor	8.1%
Unknown	4.8%

Source: ASCO 2010.

Over 80% of patients in phase 2 treated with tivozanib had a clear cell tumor histology, roughly half of patients were treatment naïve and approximately 90% of patients had favorable or intermediate risk disease using the MSKCC risk stratification criteria.

By independent review, the intention-to-treat (ITT) progression free survival (PFS) was 11.8 months, however PFS was influenced by histology and nephrectomy status. Patients with clear cell carcinoma versus all others had longer PFS of 12.5 months vs. 6.7 months, as did nephrectomized patients with PFS of 14.1 months vs. 8.2 months. Including the 176 patients who had clear cell histology and had undergone a nephrectomy, the PFS was 14.8 months.

The most commonly reported adverse events (AEs) in the phase 2 experience with tivozanib were hypertension and dysphonia at 50% and 21.7%, respectively. Other adverse events of interest were diarrhea at 12.1%, fatigue at 8.1%, stomatitis at 4.4% and hand foot syndrome (HFS) at 3.7%. Overall, 10.3% of patients required a reduction in tivozanib dose while 3.7% of patients required dose interruption.

Tivozanib Phase 1 Experience – Focus on Safety/Tolerability

Earlier tivozanib phase 1 testing was conducted at a single center in the Netherlands. The open label dose escalation trial enrolled 41 patients with solid tumors on a 28-day-on-14-day-off schema. The most commonly represented tumors were colon (n=10), renal (n=9), pancreatic (n=6), and lung (n=3), and 9 of 31 had received no prior systemic therapy. The initial tivozanib

dose evaluated was 2 mg, corresponding to one-third of the no-observed-adverse-effect-level (NOAEL) in preclinical studies, however two grade 3 events in the first two patients treated, proteinurea and ataxia, followed by a grade 4 intracranial bleed in the third patient led to a lower dose of 1.5mg being tested and 16 patients were enrolled into the 1.5mg cohort. Beyond frequent hypertension, 2 cases of grade 3/4 transaminase elevation and a grade 3 fatigue were the most notable side effects in phase 1; only one dose reduction, for a grade 3 hypertension was required. The adverse event (AE) summary is presented in figure 4.

Exhibit 5: Tivozanib Adverse Event Profile in Phase 1

Dose	All AEs	Grade 3
1.0 mg n=14	39.0%	28.0%
1.5mg n=18	62.5%	62.5%
2.0mg n=8	100.0%	71.0%

Source: AACR2008.

The incidence of hypertension for tivozanib in phase 1 ranged from 39% for the 1.0mg dose to 100% at the 2.0mg dose, with grade 3 hypertension increasing from 28% at 1.0mg to 71% at 2.0mg. The magnitude of the hypertension increase was similar for the 1.0mg and 1.5mg cohorts but clearly higher for the 2.0mg cohort. Other than grade 3 fatigue at 5%-6% no other non-laboratory adverse events (AEs) were observed at a grade 3 level. Laboratory adverse events are summarized in Exhibit 6, both in terms of total incidence and grade 3/4 if present:

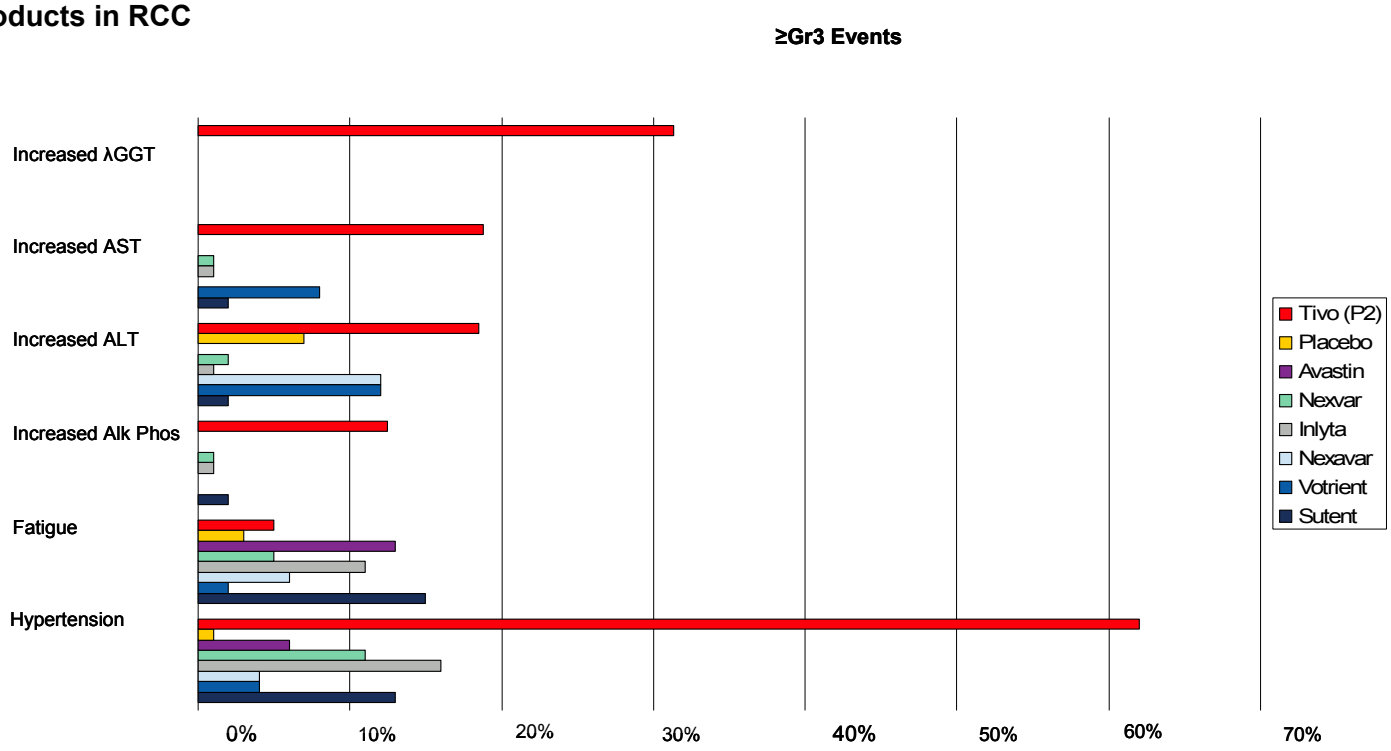
Exhibit 6: Laboratory Adverse Event Profile in Phase 1

Observation	1.0mg n=18	1.5mg n=16	2.0mg n=7
Alkaline phosphatase	17% 5.6%	50% 12.5%	42.9% 14.3%
Alanine transaminase (ALT)	33% 5.6%	25% 18.5%	42.90%
Aspartate aminotransfersase (AST)	50% 5.6%	37.7% 18.8%	42.9% 14.3%
λ-Glutamyl transferase (GGT)	27.8% 27.8%	25% 31.3%	28.6% 14.3%
Proteinurea	27.80%	43.80%	57.1% 14.3%

Source AACR 2008.

Alkaline phosphatase increases with tivozanib in phase 1 appear to be more significant in the 1.5mg and 2mg cohorts. Liver enzyme increases show no clear dose relationship, although the grade 3 toxicity is unexpected apriori for a pure VEGFR inhibitor and it may represent some degree of off-target toxicity. In this trial tivozanib half-life was estimated to be 4.4-5 days (+/- 0.3-0.6) with 4.9 days noted for the phase 3 dose. Grade 3+ adverse events (AEs) observed with tivozanib in phase 1 are compared with those reported for approved agents in RCC in the graphic below in Exhibit 7.

Exhibit 7: Comparison of Common Tivozanib Grade 3 or Higher Adverse Events Compared to Approved Products in RCC



Source: Eskens *et al.*, Clin Cancer Res, 2011 ;17 :7156-7163 and BMO Capital Markets.

Based on phase 1 data, it would appear that fatigue, a prominent feature with other tyrosine kinase inhibitors (TKIs), is less of a problem for tivozanib, although there is a wide variation in rates of grade 3/4 fatigue with approved agents. In particular, the rate of fatigue with tivozanib in phase 1 is below that reported for Sutent and Inlyta but in line with that reported for Nexavar and Votrient. The comparison with Avastin + interferon is probably not fair, based on the likely contribution of interferon to higher rates of fatigue with the combination. Of particular note from phase 1 are increased rates of liver enzyme elevations with tivozanib relative to approved tyrosine kinase inhibitors (TKI's), with rates of grade 3/4 AST/ALT elevation approaching 20% and with GGT elevations in excess of 30%. Importantly though no concomitant elevations in bilirubin were observed with tivozanib that met Hy's law criteria, although we believe that a focus on liver safety is appropriate in phase 3 based on phase 1 results.

With respect to tumor responses, 33% of patients in phase 1 showed a decrease in tumor size and five patients had stable disease for six months or longer. Six of 21 evaluable patients had

stable disease in phase 1 lasting longer than three months and included patients with esophageal cancer, parotid cancer, thyroid cancer, lung cancer, a syringioma, and a pancreatic cancer. In the colorectal cancer subset, 4 of 10 patients had stable disease lasting three months or longer.

Review of Tivozanib QTc Profile

At the recent ASCO GU symposium, AVEO presented data from a QTc trial for tivozanib in patients with solid tumors. The trial enrolled 51 patients, who received tivozanib 1.5mg/day for 21 days. The primary endpoint was QT interval corrected for heart rate using Fredericia's correction method. Baseline QT interval was assessed as the average of all six pre-dose ECG measurements on day 1 (2.5, 4, 5, 6, 8 & 10 hours post-dose). QT interval was then assessed pre-dose on days 2, 8, and 21 and 2.5, 5, and 8 hours after dosing on day 8, 2.5, 4, 5, 6, 8, and 10 hours on day 21.

Across all time points a +2.2mS increase in QTcF was observed, and on the two intensive assessment days, day 1 and day 21, the QTcF changes were -1.1mS and +6.8mS. No patients exhibited a QTcF values of >500mS although 2 patients had QTcF values of >480ms; at study entry the pre-baseline QTcF had to be < 480mS. An increase in QTcF of >60mS was observed in a single patients and six patients exhibited a change of 30-60mS. The maximal mean increase in QTcF was 9.3mS observed 2.5h after the last dose on day 21. No clinically relevant changes from baseline were observed for heart rate, PR interval, or QRS complex.

- Clinically non-significant reduction in heart rate was observed.
- No tachycardic outliers and 2 (4%) bradycardic outliers of no clinical relevance.
- 2 QRS duration outliers and overall a small effect on QRS, which is unlikely to be of clinical significance.

In addition morphologic analysis showed four patients (8%) had a new ST wave depression and four had a new T wave inversion all of which were noted to be clinically insignificant.

Tivozanib pharmacokinetics (PK) was assessed at the same time as QTc and a relationship between tivozanib serum concentration and QTcF change from baseline was observed. A linear mixed model estimated that at the average tivozanib C_{max}, an 8.27mS QTcF increase would be predicted.

Biomarker Assessment for Tivozanib

In 1Q11, AVEO listed a phase 2 open-label, single-arm trial aimed at identifying biomarkers associated with tivozanib activity in renal cell carcinoma (RCC). Both archived tumor tissue and serum biomarkers on trial will be evaluated with data expected in 2Q12. The trial listing identifies biomarkers of interest, but not limited to: CD68, HIF (hypoxia induced factor)1/HIF2, VEGF A, VEGF-B, VEGF-C, VEGF-D, HGF (hepatocyte growth factor), CAIX (carbonic anhydrase 9), and PLGF (placental growth factor).

Numerous efforts have been made to identify biomarkers in RCC that could be used to predict which patients may benefit from a particular therapy or that are at high risk for toxicity. In a recent editorial published in the Lancet Oncology, Dr. Brian Rini and colleagues have reviewed the current state of biomarker development for anti-VEGF agents in renal cell carcinoma (RCC). Of particular note, IL-8 and HIF-1α were associated with outcome in the Votrient phase 3 trial. In a Spanish study of Sutent, two polymorphisms in VEGFR3 were associated with a decrease in PFS. With respect to toxicity, polymorphisms in the CYP3A5 gene were associated with hypertension, hand-foot syndrome, and mucositis with VEGF-TKI's. The Votrient study did not report an association with VEGFR3 leading Dr. Rini and colleagues to question whether differences from biomarkers studies reflect underlying differences in biology or artifacts from small study populations.

Combination Therapy With Tivozanib

In addition to using biomarkers to optimize patient outcomes, other strategies used historically to augment the clinical impact of molecularly targeted agents have included combining agents particularly those with orthogonal mechanisms of action. For the most part such strategies have been largely unsuccessful in RCC as added toxicity appears to outweigh added efficacy. At the 2011 ASCO meeting, preliminary data from a phase 1 trial combining tivozanib + mTOR inhibitor Torisel in RCC were presented. Eligible patients could have failed 1 prior anti-VEGF therapy (71%) and received tivozanib three-weeks-on-and-one-week-off with Torisel dosed once weekly. Following a tivozanib/Torisel dose escalation to 1.5mg/25mg, 15 additional patients were added at the 1.5mg/25mg level.

The median duration of dosing in the tivozanib + Torisel combination study was 21.9 weeks, with a range from 6.9 weeks to 97.9 weeks. Three patients withdrew due to an adverse event (AE) including left ventricular dysfunction (LVD) possibly tivozanib-related, fatigue possibly related to Torisel and a patient with colitis/rectal abscess possibly related to tivozanib and/or Torisel. Two patients required dose reduction for an adverse event (AE) including one for a tivozanib related grade 2 fatigue and one for grade 3 Torisel-related hyponatremia. One unrelated cardiopulmonary death was observed on study. Torisel-related toxicity was more common with the cardinal AE of tivozanib, hypertension, only the 12th most common adverse event (AE) observed in the 1.5mg/25mg cohort. Fatigue was noted in 86% of patients (20% grade 3), stomatitis and diarrhea at 70% (7.5% and 15% grade 3), decreased appetite, nausea, constipation and dyspnea all occurred at 50%-60% with grade 3 events occurring in one patient; none for decreased appetite.

Partial responses were noted in five patients (23%), while stable disease was the most common outcome at 68% and two patients had progressive disease as best response.

While this is one of the few studies that have been completed with two novel therapies in RCC, there is still considerable toxicity, which as noted appears to be dominated by Torisel. Similarly, Negrier *et al.* published the French experience of combining Avastin with Torisel in the front line setting; Lancet Oncology: Jul;12(7):673-80, 2011. The authors concluded that "The toxicity of the temsirolimus and bevacizumab combination was much higher than anticipated and limited treatment continuation over time." Currently the CALGB is conducting

a phase 3 trial evaluating the combination of Avastin + Novartis's m-TOR inhibitor, Afinitor with data expected in 1Q13.

Tivozanib Beyond RCC - Colorectal Cancer

The most significant investment for tivozanib beyond RCC is in metastatic colorectal cancer (mCRC). In 4Q11, AVEO and partner Astellas initiated a 252-patient phase 2 trial, BATON, to compare tivozanib to Avastin on a background of FOLFOX chemotherapy in patients with untreated metastatic colorectal cancer. The primary endpoint of the trial is progression free survival (PFS) with data expected in 4Q14.

Current standard of care for treatment of metastatic colorectal cancer (mCRC) involves frontline use of Avastin + FOLFOX, dosed sometimes through progression into the second line, subsequent use of anti-EGFR antibodies Erbitux or Vectibix as preferred second line options and in some cases as frontline alternatives to Avastin, and then investigational agents for third line disease. For those patients that receive Erbitux or Vectibix frontline, Avastin is used second line, typically in combination with FOLFOX or FOLFIRI. Recently Regeneron demonstrated a progression free survival (PFS) and overall survival (OS) benefit with its VEGF-TRAP ZALTRAP in second-line mCRC and is seeking approval in 2012. More recently Onyx and partner Bayer reported a statistically significant improvement in overall survival (OS) with VEGF-multikinase inhibitor regorafenib as a third-line treatment option in patients with mCRC, and an NDA filing is expected in 1H12.

Astellas Agreement

Under the Astellas collaboration agreement, AVEO received an initial cash payment of $125 million, comprised of a $75 million license fee and $50 million in research and development funding. AVEO expects to retain net proceeds of approximately $96 million of the initial cash payment from Astellas, after payments to Kirin Kyowa Hakko and strategic, legal, and financial advisors. AVEO is also eligible to receive from Astellas an aggregate of approximately $1.3 billion in potential milestone payments relating to development and commercialization milestones for tivozanib. In addition, if tivozanib is successfully developed and launched in royalty bearing territories, Astellas will be required to pay to AVEO tiered, double-digit royalties on net sales. AVEO is required to pay to Kirin Kyowa Hakko a specified percentage of milestones and royalties received from Astellas. Within the next 18 months, AVEO expects to receive $90 million in milestones related to the US and ex-US regulatory filings and approvals.

Competitive Landscape in RCC

With the recent approval of Pfizer's Inlyta, FDA has now approved seven targeted therapies for patients with advanced renal cell carcinoma (RCC). These include the VEGR-TKIs Sutent, Nexavar, Votrient and Inlyta, the anti-VEGF antibody Avastin and the m-TOR inhibitors, Torisel and Afinitor. The four VEGF-TKIs are the clearest competitors to tivozanib and key characteristics of the approvals are summarized below in figure 7.

Exhibit 8: Key Characteristics of TKI's Approved for RCC -1

Drug Key Trial	Dose	Patients	Metabolism
Sutent vs IFN N=735	50mg/d 4 weeks on 2 weeks off	Favorable - 34-38% Intermediate - 56-59% Poor - 6-7%	CYP3A4
Votrient vs placebo n=435	800mg/d	Favorable - 39% Intermediate - 53-55% Poor - 3%	CYP3A4, with minor contributions from CYP1A2 and CYP2C8
Nexavar vs placebo N=769	400mg bid		CYP3A4 and UGT1A9 glucuronidation
Inlyta vs Nexavar N=723	5-10mg bid	Favorable – 41-44% Intermediate – 55-58% Poor – 1% Prior Sutent – 54% Cytokines – 35% Avastin - 8% Torisel – 3%	CYP3A4/5, to a lesser extent CYP1A2, CYP2C19, and UGT1A1

Sources: FDA and BMO Capital Markets.

For purposes of FDA approval, two drugs, Votrient and Nexavar were compared with placebo, while both Sutent and Inlyta used active controls, interferon, and Nexavar, respectively. Sutent and Votrient are dosed once-daily, while Inlyta and Nexavar are dosed twice daily. Daily doses range from 10mg for Inlyta to 800mg for Nexavar and Votrient and in part reflect relative activity against VEGF receptor signaling as noted earlier. Of the 4 VEGF-TKIs, Sutent dosing is uniquely characterized by a 4 week-on-2-week-off regimen. All four agents are metabolized primarily by cytochrome 3A4 with glucuronidation playing a role in Nexavar and Inlyta

metabolism. Inlyta's approval was based on a trial enrolling patients, who had received a prior systemic therapy which in 65% of cases was an anti-VEGF agent.

The following table summarizes key safety and efficacy parameters for the four approved VEGF-TKIs. The primary endpoint of VEGF-TKI registration trials was PFS, which ranges in the VEGF naïve patients from 6 to 11 months. Due to cross-over and salvage therapy, an overall survival (OS) benefit of an anti-VEGF inhibitor over a non-VEGF control can not be estimated, but absolute overall survival (OS) is around two years.

Exhibit 9: Key Characteristics of TKI's Approved for RCC -2

Drug	PFS Test vs contol OS	ORR Duration of Response	BBW	Warnings & Precautions	AE leading to discontinuation	Duration of dosing Dose modification
Sutent	11.0 mo. vs 5 mo. 26.4 mo. vs 21.81mo.	31% vs 6% >13 months	Hepatic toxicity	Hepatotoxicity Pregnancy Left Ventricular Dysfunction QT Prolongation and Torsades de Pointes Hypertension Hemorrhage Thyroid dysfunction Wound healing Adrenal function Laboratory Tests	20% vs 24%	11.1 mo. vs 4.1mo 54% vs 39% dose interruption 52% vs 27% dose reduction
Votrient	9.2mo vs 4.2 mo	30% vs 3% 14.5mo.	Hepatic toxicity	Hepatic Effects QT Prolongation & Torsades de pointes Hemorrhagic Events ATE GI Perforation & fistula Hypertension Wound Healing Hypothyroidism Proteinuria Pregnancy	14% vs 3%	7.4 mo. 42% dose interruption 36% dose reduction
Nexavar	5.9 mo vs 2.8 mo	2.1% 1.9mo	None	Cardia Ischemia Hypertension Dermatologic toxicity GI perforation Warfarin Wound Healing Complication QT Interval Prolongation	10% vs 8%	4.5 mo vs 2.3 mo 24% vs 6% dose inerrupted or reduced
Inlyta	6.7 vs 4.7mo NR vs 18.9mo	19% vs 9% 11mo vs 10.6mo	None	Hypertension and Hypertensive Crisis ATE VTE Hemorrhage GI Perforation and Fistula Formation Thyroid Dysfunction Wound Healing Complications PLES Proteinuria Elevation of Liver Enzymes Hepatic Impairment Pregnancy	9% vs 13%	6.4mo vs 5.0 mo. 55% vs 62% dose interruption or delay

Sources: FDA and BMO Capital Markets.

Specific review of VEGF-TKI efficacy data from pivotal studies suggests greatest anti-tumor effect with Sutent and Votrient, followed by Inlyta and then Nexavar. Overall response rates (ORRs) of 31% and 30% for Sutent and Votrient, respectively, appear comparable and while a 19% response rate for Inlyta appears lower, it should be noted that this was from a more advanced second line RCC population and that phase 2 data suggest ORR of ~40%. With a 2.1% overall response rate (ORR), Nexavar is clearly the least potent VEGF-TKI in RCC, with primary benefit on disease stabilization. Differences between agents in progression free survival (PFS) seem to track with anti-tumor efficacy and show Sutent having the longest PFS at 11 months, followed by Votrient at 9 months, Inlyta at 6.7 months, and Nexavar at 5.9 months. Overall, we see a ~5 month difference in PFS between frontline standard of care Sutent and salvage agent Nexavar.

One of the key differences between the four approved TKI's is the presence or absence of a black box warning with both Sutent and Votrient carrying a black-box warning for hepatic toxicity. Each agent carries a long list of Warnings and Precautions with hepatic, cardiorenal, and wound healing common to each. Nexavar is notable for the dermatologic toxicity warning.

Reviewing discontinuation rates due to toxicity provides another perspective on relative tolerability of approved VEGF-TKI's, and while acute toxicities occur independently of the duration of dosing, the impact of dosing duration needs to be taken into consideration for cumulative toxicity. In addition it is not unreasonable to assume that drugs approved more recently may benefit from the medical oncology community's collective learning on prevention and management of expected toxicity. Taking all of these variables into consideration, we view all approved TKIs as having very similar discontinuation rates:

- 20% of patients discontinued Sutent due to an adverse event (AE) over an 11-month dosing period;
- 14% of Votrient patients discontinued dosing due to an adverse event (AE)over a 7-month period,
- 10% of Nexavar patients discontinued dosing due to an adverse event (AE) over a 4.5-month period, and
- 9% of Inlyta patients discontinued dosing due to an adverse event (AE) over 6.4-month of dosing.

Another approach to assessing tolerability of VEGF-TKIs is to examine the proportion of patients that require dose interruption or reduction of dosing. In this respect, the Nexavar registration study seems to stand out as 25% of patients required dose interruption or reduction, a rate that is approximately half that observed for Sutent and Votrient. The Inlyta trial enrolled a primarily second-line population and while one might conclude that patients with acute-VEGF related toxicities would not have been enrolled the 55% dose interruption/reduction for Inlyta, and 62% dose interruption/reduction for Nexavar perhaps suggest that toxicities were more commonly observed in the second-line population.

Beyond competing with current agents, the development landscape behind tivozanib needs to be assessed. The development-stage landscape is limited with most focus in three areas:

- Adjuvant therapies – Sutent, Nexavar and Votrient are in phase 3 testing
- Second line – Novartis is conducting studies of an FGFR3 centric TKI, dovitinib (TKI-258) and Afinitor/Avastin combination studies
- Vaccines – Immatics is adding IMA901 to Sutent in the front line setting and Argos is adding dendritic cell vaccine AGS-003 to Sutent in the frontline setting as well.

It is also noteworthy that GSK has two phase 3 trials of Votrient compared to Sutent in the front line setting, COMPARZ and PICES, while Pfizer is conducting the AGILE trial of Inlyta vs. Nexavar. Details of these 3 frontline head-to-head studies include:

- COMPARZ n=927, data expected 3Q12, primary endpoint is PFS
- PICES n=169, data expected 2Q12, primary endpoint is patient preference
- AGILE, n=447, data expected 2Q12, primary endpoint is PFS

While development-stage threats to tivozanib appear limited, ongoing Votrient and Inlyta trials may be more important. GSK's Votrient will have head-to-head data against Sutent in 2012. In addition to clarifying the relative toxicities of these two agents, GSK, unlike AVEO and Astellas will be able to make statements regarding the comparative efficacy with the de facto standard of care in frontline RCC. While the AGILE trial of Inlyta will not supply head-to-head data with Sutent it will characterize the tolerability of Inlyta in a population that has not been exposed to prior anti-VEGF therapy and will allow for a relative comparison to TIVO-1 in terms of magnitude of benefit over Nexavar.

Inlyta

Inlyta was recently approved by FDA for use in patients failing one prior systemic therapy. In the cytokine only patients, Inlyta produced a 12-month PFS, which is clearly competitive to approved VEGF-TKIs.

The AXIS phase 3 trial compared Inlyta to Nexavar in the second-line setting. The AXIS trial was developed following two phase 2 trials in the second-line setting:

- In cytokine refractory RCC, Inlyta produced a 44% ORR with a 15.7 month TTP, *Rixe et al.,* Lancet Oncology 2007, 8: 8975-84.
- In the TKI refractory setting, overall response rate (ORR) was 23% and PFS was 7.4 months., Rini *et al.* Journal of Clinical Oncology 2009, 27L 4462-68.

Eligible patients for the AXIS trial had failed one prior treatment including one of either: Sutent, Avastin, Torisel, interferon or another cytokine. Patients were randomized to Nexavar or Inlyta with the dose of Inlyta escalating from 5mg/bid to 10mg/bid if tolerated. The primary endpoint of AXIS was progression free survival (PFS) with tumor assessment performed after 6

weeks, 12 weeks, and every 8 weeks thereafter. One of the key secondary endpoints in AXIS was quality of life (QOL) assessed every 4 weeks, at the end of therapy and 28 days following the last dose. Quality of life (QoL) was assessed using the Functional Assessment of Cancer Therapy Kidney Symptoms Index (FSKI) as well as with the EuroQoL 5D.

The AXIS trial was designed with 90% power to demonstrate a two-month absolute increase in PFS from five months assumed for Nexavar to seven months for Inlyta. The trial did demonstrate a two-month PFS increase from 4.7 months with Nexavar to 6.7 months with Inlyta by independent review (HR 0.665). By prior regimen, PFS in the Inlyta arm ranged from 4.2 months to 12.1 months and for the Nexavar arm from 4.3 months to 6.5 months, as noted below in Exhibit 10.

Exhibit 10: PFS Gated by Prior Therapy

Prior Therapy	Inlyta	Nexavar
Cytokines n=251	12.1mo.	6.5mo.
Sutent n=389	4.8mo.	4.3mo.
Torisel n=24	10.1mo.	5.3mo.
Avastin n=59	4.2mo	4.7mo.

Source: ASCO 2011.

Only for prior cytokine or Sutent use did the Inlyta PFS benefit achieve statistical significance, although the clinical significance of the benefit in the Sutent population is negligible. Adjudicated response rate data favored Inlyta at 19.4% vs. 9.4% for Nexavar.

With respect to tolerability, only one-third of patients could dose-escalate Inlyta to 10mg bid. A further one-third of patients decreased dose in the Inlyta arm, although this was less than Nexavar at 52% dose reduction. Dose interruptions were noted in 54% and 63% of Inlyta and Nexavar treated patients, respectively, with discontinuations due to an investigator assessed adverse event (AE) of 3.9% and 8.2%, respectively.

Exhibit 11: Adverse Event Summary

Event	Inlyta (All/ Grade 3/4) %	Nexavar (All/ Grade 3/4) %
Diarrhea	55/11	53/7
Hypertension	40/16	29/11
Fatigue	39/11	32/5
Nausea	32/3	22/1
Vomiting	24/3	8/0
Hypothyroidism	19/<1	8/0
Stomatitis	15/1	12/4
Hand foot syndrome	27/5	51/16
Rash	13/ <1	32/4
Alopecia	4/0	33/0

Source ASCO 2011.

In the AXIS study hypertension and hypothyroidism were more commonly observed with Inlyta, while hand foot syndrome (HFS), rash and alopecia were more commonly observed with Nexavar. Gastrointestinal (GI) toxicity and fatigue were commonly observed with both agents. Common laboratory abnormalities are summarized below in Exhibit 12:

Exhibit 12: Laboratory Adverse Event Summary

Event	Inlyta (All/ Grade 3/4) %	Nexavar (All/ Grade 3/4) %
Neutropenia	6/1	8/1
Anemia	35/<1	52/4
Thrombocytopenia	15/<1	14/0
Lymphopenia	33/3	36/4
Hypophosphatemia	13/2	50/16
Hypercalecemia	30/4	7/0
Hypocalcemia	10/1	28/1
Elevated Hgb	9	
Elevated Lipase	27/5	46/15

Source ASCO 2011.

Cytopenias were observed with both agents in the AXIS study but the incidence of grade 3 or 4 cytopenias was low as was the incidence of other laboratory abnormalities. The tolerability of Inlyta was similar to that of Nexavar, with some exceptions. Common adverse events seen with Inlyta, such as diarrhea, hypertension, and fatigue, have been noted with other VEGFR inhibitors. Other adverse events often seen with the currently approved VEGFR inhibitors that were less commonly reported with Inlyta included HFS, cutaneous toxicities, and myelosuppression.

Quality of life (QoL) in AXIS was assessed using a 15-item scale, the FKSI as well a 9-item subset assessing disease-related symptoms using the FKDS tool. The 15 items included in the FKSI are: lack of energy, bone pain, shortness of breath, coughing, hematuria, bothered by fevers, pain, fatigue, loosing weight, appetite, side effects, enjoying life, worsened condition, ability to work and sleep. The first 9 items are included in the FKDS. Clinically meaningful changes were considered five points for the FKSI and three points for the FKDS.

Completion of QoL data was accomplished by ~ 90% of patients at each visit where QoL was assessed, however, patient dropouts meant that by cycle 6 for example only 50%-60% of patients originally enrolled were eligible to complete a QoL assessment and this fell to 20%-30% by cycle 13 at week 52. Patients completing forms showed that QoL was stable to slightly increasing for Inlyta during the study and while numerically, patients reported better QoL from the Inlyta arm, especially for the 9-item scale there was a lot of overlap between the two treatments.

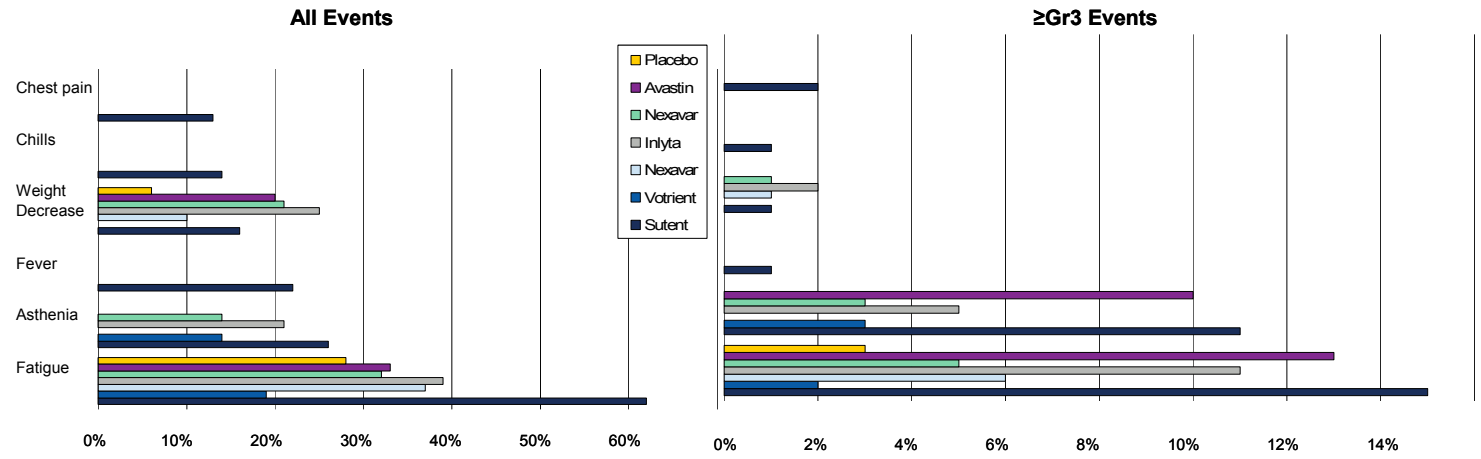
In a composite analysis of time to death, progression or worsening of symptoms (FKSI) the data suggest a small statistically significant benefit favoring Inlyta at 3.1 month vs. 2.8 months for a 17% reduction in risk. Using the FKDS the difference between the two drugs increased to 0.8 months in favor of Inlyta. Interestingly QoL improved once patients stopped taking either agent, even in the context of progressive disease.

In a discussion of these data at ASCO, the presenter noted that while the PFS data for Inlyta in the second-line cytokine refractory setting are as good as any published, they are perhaps less robust in the prior VEGF patients. In the pivotal Afinitor trial conducted by Novartis, a PFS of 4.9 months was observed in the context of more than 80% of patients having received two or more prior regimens including Sutent for 50% and 25% having received both Sutent and Nexavar. In this context the 4.8 month PFS posted by Inlyta is less impressive. Further in a retrospective analysis of patients receiving sequential VEGF therapy the time to treatment failure of the first line VEGF was 10.5 months while that for the second line was 4.9 months, Vickers *et al*. Urology 76 430-435 2010.

Establishing Tolerability/Safety Benchmarks for TIVO-1

With AVEO highlighting superiority safety and tolerability as a primary advantage of tivozanib over other less selective VEGF- targeted agents currently approved for RCC, we have sought to more fully characterize the safety and tolerability profile of each of these agents to provide context for full TIVO-1 data expected at ASCO. Based on our review of prescribing information, we have established what we believe to be an appropriate context for evaluating tivozanib safety and tolerability from the TIVO-1 ahead of release at ASCO in June. In our review, we have categorized adverse events (AEs), both overall and by grade 3+, according to organ system, with particular focus on constitutional AEs, gastrointestinal AEs, cardiorenal AEs, dermatologic AEs, MSK/CNS AEs, and hematologic and respiratory AEs. We have also looked at laboratory abnormalities broken down by gastrointestinal laboratory AEs, renal/metabolic laboratory abnormalities, and hematology laboratory abnormalities.

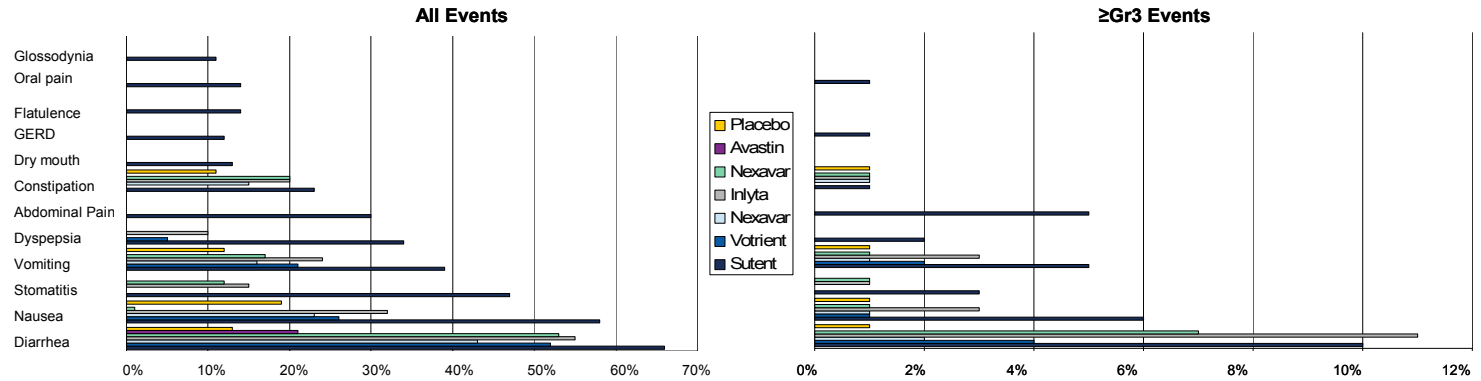
Exhibit 13: Incidence of Constitutional Adverse Events



Sources; FDA and BMO Capital Markets.

Based on data from the package inserts, the placebo data suggest that, using a cut off of 10%, fatigue and weight decrease are commonly observed constitutional symptoms of RCC in general. Focusing on fatigue in the left data panel it would appear that with the exception of Sutent and Votrient, active therapies marginally increase the occurrence of fatigue. Sutent clearly increases fatigue significantly, while Votrient appears to reduce fatigue. Drilling down to grade 3+ fatigue in the right hand panel, the placebo data suggest that roughly 3% of RCC patients suffer from severe fatigue and that active therapy with Nexavar doubles the risk, increasing 3-4 fold with Inlyta, Avastin/IFN and Sutent. Once again, severe fatigue rates appear lower for Votrient. The other most commonly observed constitutional side effect is weight loss, where the risk once again appears to be higher for active therapy compared to placebo and for grade 3+ weight loss the risk is 1%-2%. Other noteworthy constitutional side effects with anti-VEGF therapy include asthenia or energy loss. Roughly 10%-20% of patients receiving active therapy suffer from asthenia and for 1 in 10 patients receiving Sutent or Avastin/IFN asthenia will be at grade 3 or higher.

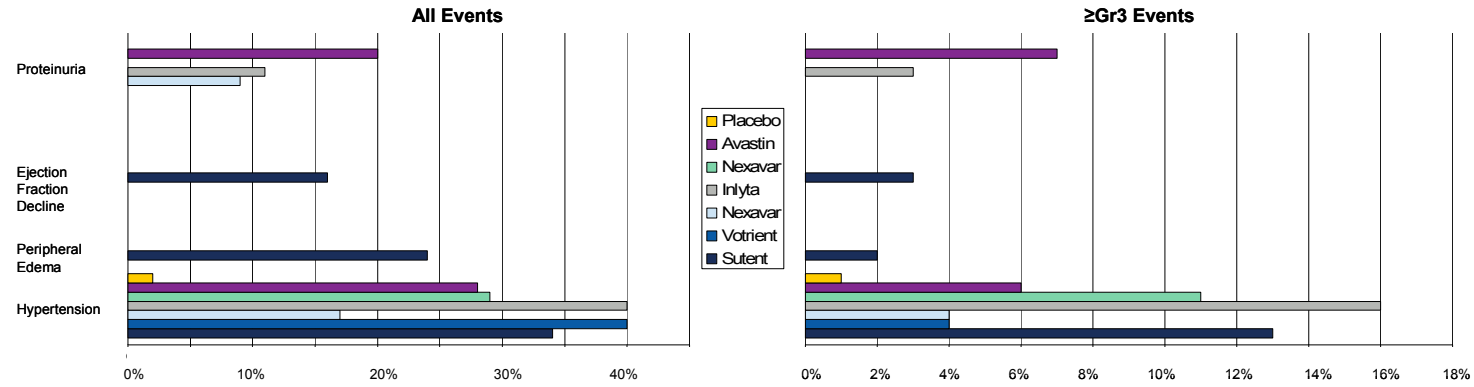
Exhibit 14: Incidence of Gastrointestinal Adverse Events



Sources: FDA and BMO Capital Markets.

Gastrointestinal side effects are commonly observed in renal cell carcinoma (RCC) patients and once again using placebo data as an index, 10%-20% of patients receiving placebo suffer from constipation, nausea, vomiting and diarrhea, but rarely does this occur at grade 3 or higher as noted in the right hand panel. VEGFR-TKIs increase the incidence of diarrhea with 50% or more patients reporting some diarrhea. With respect to grade 3 or higher diarrhea, the data suggest that patients receiving Votrient or Nexavar are 2-3 times more likely to suffer severe diarrhea increasing to 1 in 10 patients receiving Inlyta or Sutent. With the exception of constipation, there is a suggestion that GI side effects are both more common and more severe with Sutent and Inlyta than Nexavar or Votrient.

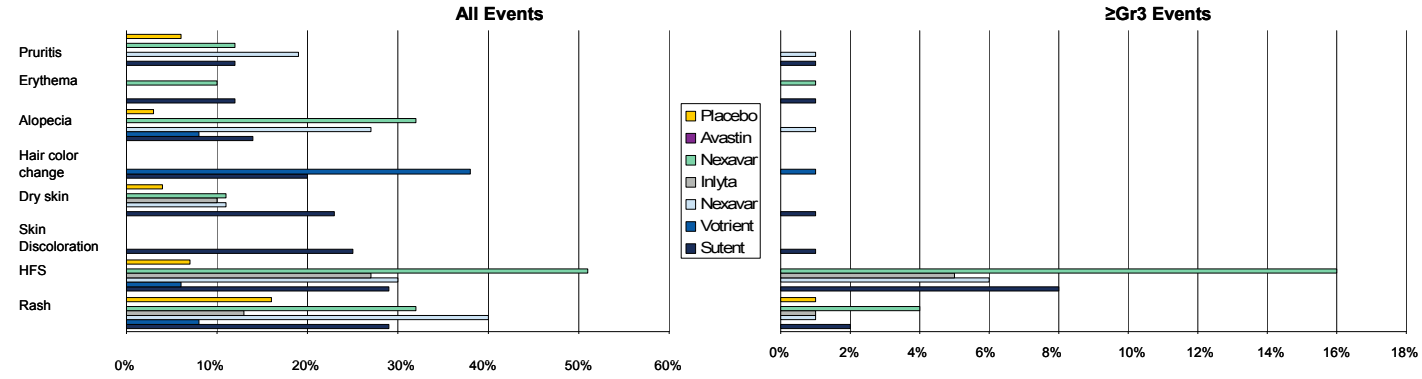
Exhibit 15: Incidence of Cardiorenal Adverse Events



Source: FDA and BMO Capital Markets.

The cardinal side effect of VEGF inhibition is hypertension which occurs in 30%-40% of patients treated with Avastin. Severe hypertension is also observed in 4%-16% of patients with Inlyta appearing to carry the highest risk for hypertension. Only in the Sutent Product Insert are peripheral edema and decline in ejection fraction listed as both common and serious cardiovascular side effects. FDA's review of Sutent notes that 21% of patients receiving Sutent versus 11% receiving interferon (IFN) had a left ventricular ejection fraction (LVEF) decline below the lower limit of normal according to the treating institution's guidelines. A baseline abnormal LVEF was noted in 5 of 78 Sutent treated patients, suggesting that the LVEF decline was treatment-related. FDA noted that while CHF or left ventricular dysfunction was relatively rare in the study, it was more commonly observed in the Sutent arm as was the incidence of peripheral edema. Proteinuria was also noted in some studies, with a suggestion that Avastin is associated with a higher risk.

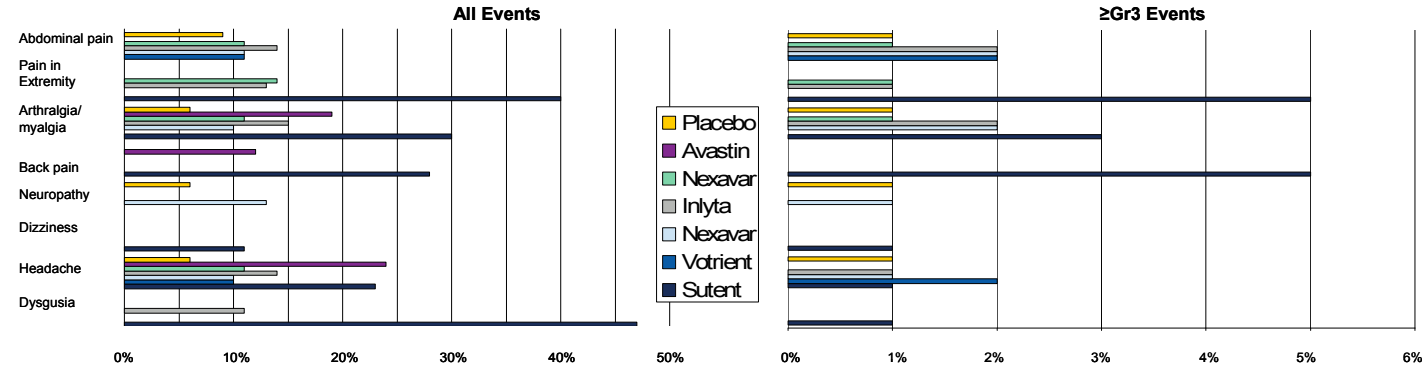
Exhibit 16: Incidence of Dermatologic Adverse Events



Sources: FDA and BMO Capital Markets.

Patients with RCC receiving placebo report a low level of a variety of dermatologic toxicities, however, Nexavar has the most distinct dermatologic toxicity profile with rash, hand foot syndrome (HFS), and alopecia reported in more than 30% of patients. Sutent also has a distinct dermatologic profile with skin discoloration, dry skin, hair color change reported in addition to rash and HFS. Apart from HFS, Inlyta appears to have a more moderate dermatologic toxicity profile compared to Sutent. Votrient for the most part has the least dermatologic toxicity, though hair color change appears to be a distinctive toxicity.

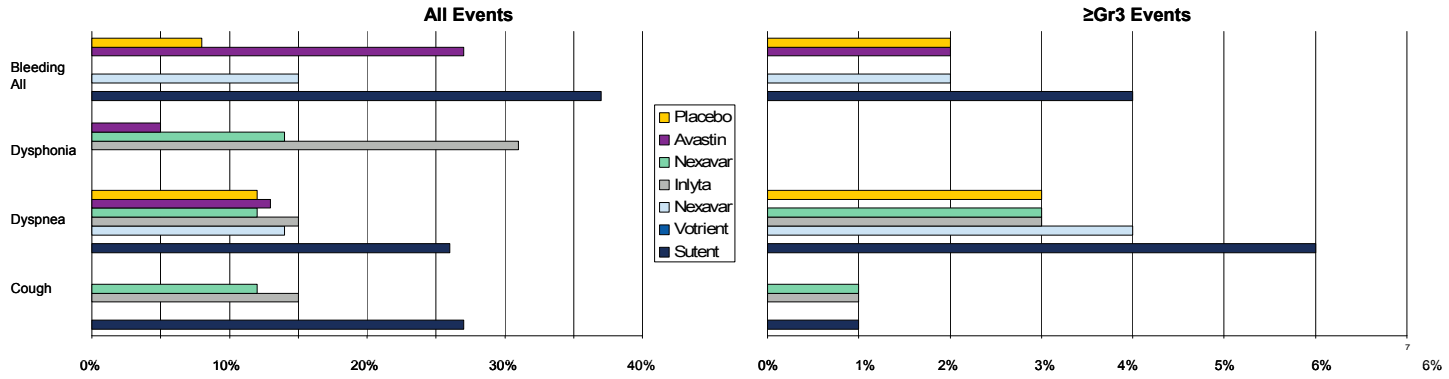
Exhibit 17: Incidence of Musculoskeletal or Neurologic Adverse Events



Source: FDA and BMO Capital Markets.

Less than 10% of placebo treated patients reported pain including headache and while VEGF antagonists increase the occurrence of neurological and musculoskeletal events, grade 3 or higher events were only reported for Sutent.

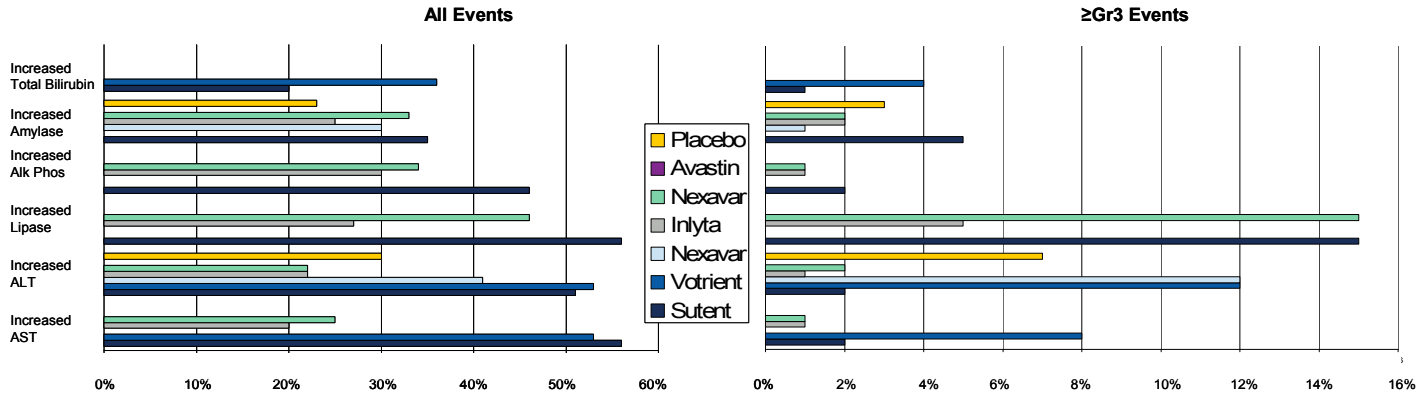
Exhibit 18: Incidence of Bleeding or Respiratory Adverse Events



Source: FDA and BMO Capital Markets.

Bleeding as an adverse event (AE) covers a number of different bleeding types, however it is apparent that bleeding and wound healing problems are common in patients treated with anti-VEGF agents. Severe bleeds while uncommon, rare events can be catastrophic. The respiratory system is relatively spared by anti-VEGF therapy with the exception of dysphonia which is common in patients receiving Inlyta.

Exhibit 19: Incidence of Laboratory AEs – Gastrointestinal Adverse Events

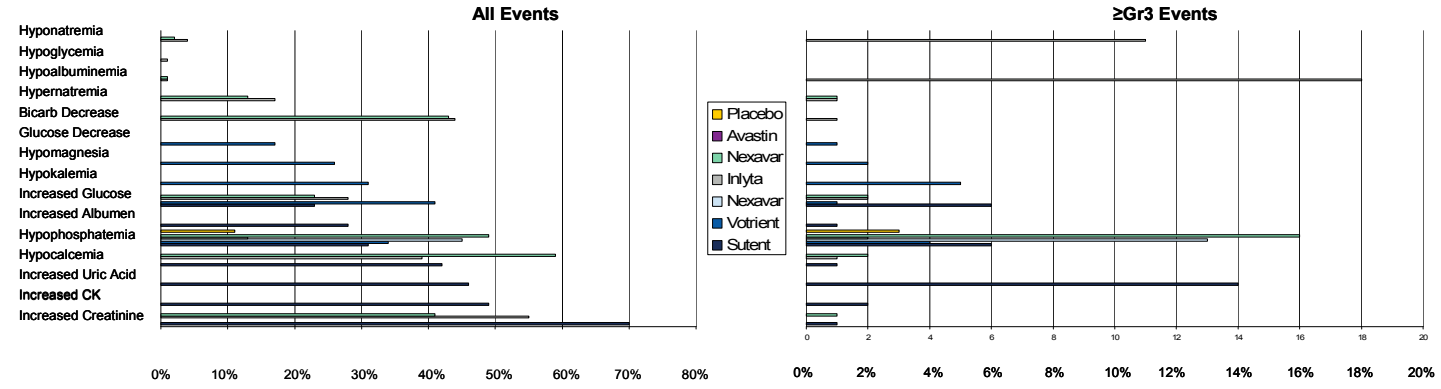


Source: FDA and BMO Capital Markets.

Focusing on laboratory events and specifically those that relate to gastrointestinal systems, placebo data suggest that renal cell carcinoma (RCC) patients have a 20%-30% incidence of increased amylase and increased alanine aminotransfersase (ALT). VEGF antagonists appear to lead to a broad range of GI-related laboratory events and most notable are grade 3 or higher ALT, AST and bilirubin changes. FDA regards ALT changes as more indicative of hepatic injury. Specifically for Votrient, FDA notes that in 34 of 36 patients with grade 3 or higher ALT, levels reversed upon cessation of drug but in two cases patients went on to develop hepatic failure. Given the incidence of grade 3 or higher bilirubin increase, FDA tested for cases of Hy's law defined **as a concurrent elevation in ALT > 3xULN and total bilirubin > 2xULN with no evidence of biliary obstruction or of other causes that can reasonably explain the elevation as evidenced by normal or <3 X ULN of alkaline phosphatase. FDA screened 990 patients receiving Votrient monotherapy identifying 4 cases of Hy's law all from the**

renal cell population (n=593), three of which were identified in the pivotal trial. Death due to hepatic injury occurred in 3 of 4 patients.

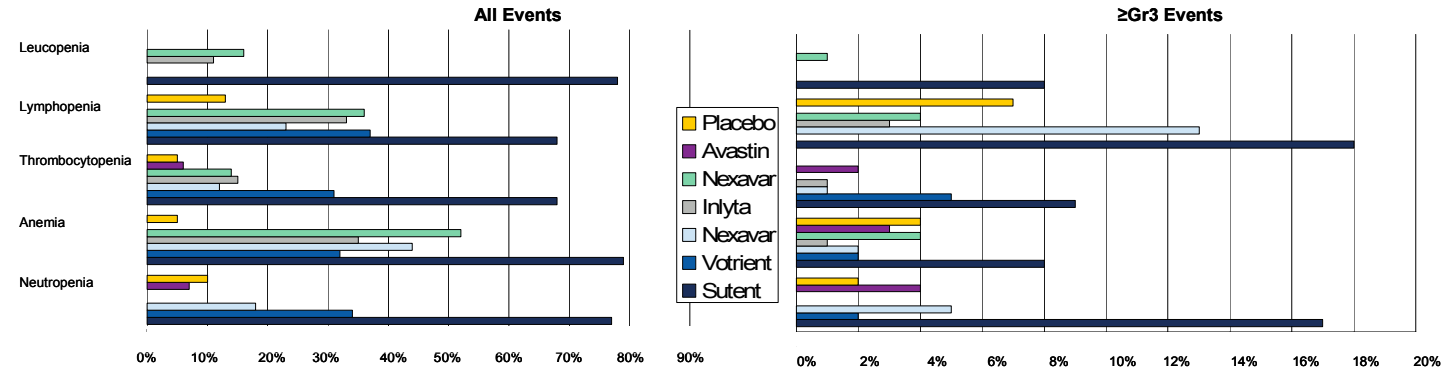
Exhibit 20: Incidence of Laboratory AEs – Renal or Metabolic Adverse Events



Source: FDA and BMO Capital Markets.

The Product Inserts of approved anti-VEGF therapies for RCC list an array of renal and metabolic laboratory adverse events (AEs). Notably, placebo treated patients have a low incidence of hypophosphatemia.

Exhibit 21: Incidence of Laboratory AEs – Hematologic Adverse Events



Source: FDA and BMO Capital Markets.

Approximately 10% of placebo-treated RCC patients have some degree of hematologic insufficiency and for the most part, the anti-VEGF agents increase both incidence and severity. With the exception of neutropenia, Avastin appears to have little to no impact on hematopoiesis. Nexavar, Votrient and with the exception of grade 3 of higher lymphopenia, Inlyta modestly increase incidence of hematologic toxicity but not severity. The exception is clearly Sutent as roughly three-fourths of patients can expect some degree of hematologic toxicity which in 10%-20% of cases will be grade 3 of higher. Sutent's inferior hematologic toxicity profile is assumed to relate to its inhibition of the flt3 tyrosine kinase activity.

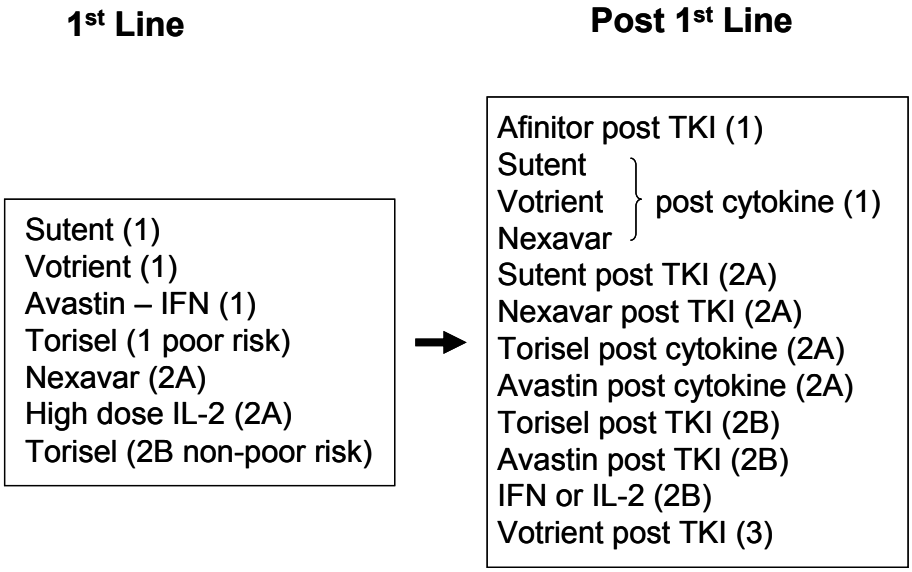
RCC Market

According to the National Cancer Institute (NCI) 60,920 Americans were diagnosed with and 13,120 died from renal cell carcinoma (RCC) in the US in 2011. The rate of RCC is increasing by 2% per year. With respect to histology, approximately 90% of renal cell tumors are comprised by renal cell carcinoma and of these 85% are clear cell tumors.

As noted previously, since 2005 FDA has approved 7 targeted therapies for RCC starting with Nexavar in 2005 and followed by 4 other VEGF targeted agents: Sutent (Pfizer, 2006), Avastin and Votrient (Roche and GSK, 2009) and Inlyta (PFE, 2012). In addition two m-TOR inhibitors have been approved for RCC: Torisel (PFE, 2007) and Afinitor (Novartis, 2009).

NCCN's 2012 guidelines, which predates the Inlyta approval suggests that Sutent, Votrient, or Avastin with interferon are supported by the highest level of evidence in the front line setting for treatment of RCC. In keeping with the design of the Torisel pivotal trial, NCCN adds Torisel as an option for patients with MSKCC high-risk disease. Following progression on one of these agents, NCCN recommends Afinitor. NCCN also notes that Sutent, Votrient or Nexavar have high level evidence for benefit in patients progressing on cytokines, though this population no longer exists in the US.

Exhibit 22: NCCN Treatment Guideline for Clear Cell Renal Cell Carcinoma V2012.1



Source: NCCN & BMO Capital Markets

BMO Capital Markets estimates that between 60% and 80% of renal cell carcinoma patients are treated in the community setting and that community oncologists, on average treat less than five patients with metastatic disease per year. With so few patients, community oncologists have shown allegiance to Sutent, which is still the dominant therapy. Despite the fact that Votrient has a superior tolerability profile than Sutent, RCC expert feedback oncologists both academic and community-based await data from the ongoing head-to-head trial before deciding if Votrient replaces Sutent as the therapy of choice. Expert feedback also suggests that the duration of therapy in the community is also reported to be less than six months compared with around 12 months in clinical trials. This difference is multi-factorial but factors include:

- Side effects – community oncologists do not treat enough patients with Sutent on an annual basis to develop expertise with managing side effects.
- Progression – renal cell carcinoma patients are followed by scans every 2-3 months, and it is likely that the threshold for progression is lower in the community than in academic centers.
- Non-trial patients – as noted before, a proportion of patients treated would not have been eligible for inclusion in a clinical trial and these patients are likely to be less able to tolerate Sutent.

Ficlatuzumab (HGF/c-met)

AVEO's second pipeline candidate in oncology, behind tivozanib, is ficlatuzumab, an antibody to hepatocyte growth factor (HGF). Ficlatuzumab was originally partnered with Schering-Plough (SGP) but was returned to AVEO following the merger of SGP with Merck. HGF or its more descriptive name scatter factor (SF) is the sole ligand binding to the c-MET receptor. In cell culture, SF causes cell morphology to change and cells to scatter. The receptor, c-MET or mesenchyme epithelial transition factor is named to reflect the ability of SF to cause a transition between epithelial and mesenchymal phenotypes, a key step in the oncogenic pathway. As an oncogene, c-MET signaling through the PI3K/Akt pathway promotes cancer cell survival, though the PI3K/STAT/JNK pathway EMT transformation, through Src/FAK increases cellular motility and invasion, and through RAS/RAF/MAPK cellular proliferation. Given the broad range of signaling intermediates touched by c-MET there is also considerable potential for cross talk between c-MET and other receptors.

Given its role in tissue development, the c-MET receptor is broadly expressed in numerous organs. With respect to cancer, c-MET can become amplified leading to over expression and constitutive activation as has been shown in gastric cancer, esophageal cancer and liver metastases from colorectal cancer for example. Mutations in c-Met are known to occur in smokers making it distinct from other receptors such as EGFR and ALK which are found to be mutated exclusively in non-smokers. Differences in c-Met mutations patterns are also observed with different lung cancer histologies and in different patient ethnicities.

Dysregulation of c-Met is also known to occur as an escape mechanism during tumor progression. The clearest example of this occurs in non-small cell lung cancer (NSCLC), where c-Met activation develops as an escape pathway for Tarceva or Iressa treated NSCLC cells. MET amplification as a mechanism for acquired Tarceva/Iressa resistance has been document in approximately 20% of NSCLC patients.

HGF is ubiquitously expressed and is frequently over-expressed in the stroma surrounding tumors suggesting a potential role for local paracrine activation of c-Met bearing tumor cells. Over-expression of HGF by tumor cells has also been observed, which with expression of c-Met on the same tumor cell provides evidence for autocrine signaling.

Inhibition of c-Met signaling has two potential benefits in oncology:

- Controlling tumor growth in tumors with c-Met oncogene addiction where inhibition of c-Met has potential to be a primary therapy
- Reducing tumor spread and metastasis, a process termed oncogene expedience, where inhibition of c-Met has the potential to reduce metastatic spread and play a role in the adjuvant setting.

Phase 1 Ficlatuzumab Data

Ficaltuzumab is one of three antibodies targeting the Met pathway in advanced clinical development. Roche's anti-cMet antibody, onartuzumab (metMAB) is currently in phase 3 testing while AMGN's AMG 102, like ficlatuzumab an antibody to HGF is in phase 2.

At the 2011 ASCO meeting, AVEO presented data for ficlatuzumab combined with Iressa in NSCLC patients of Asian ethnicity. In the study Ficlatuzumab was dosed at 10mg/kg or 20mg/kg every 2 weeks with 250mg/day Iressa. A total of 15 patients were enrolled in the study with 3 patients receiving the lower dose of ficlatuzumab and with 12 patients receiving the higher dose. All three patients at the lower dose and seven patients at the higher dose had received prior EGFR TKI therapy.

Ficlatuzumab was reported to be well tolerated with three grade 3 adverse events and one grade 4 serious adverse event. The grade 3 events included two possibly related to ficlatuzumab, including a paranychia and a case of peripheral edema and one probably related to ficlatuzumab which was a case of acneform dermatitis. The grade 4 event, a case of diffuse alveolar damage was possibly related to ficlatuzumab. The average duration of therapy at the low dose was 4 weeks, increasing to 14 weeks at the high dose. Objective responses were limited to the high dose arm and included four complete responses (CRs) which with a single partial response (PR) produced an overall response rate (ORR) of 33%. In addition, four patients exhibited stable disease as best response. The serum half-life of ficlatuzumab was estimated to range from 11-23 days with half-life increasing with extended dosing duration. After two days of ficlatuzumab dosing, serum levels of HGF increased suggestive of ficlatuzumab induction.

Based on these data, AVEO has initiated an open label randomized trial evaluating Iressa with or without ficlatuzumab in previously untreated Asian never or light smoker patients who are presumed to have a high likelihood of harboring tumors with an activating EGFR mutation. Light smokers are defined as having quit smoking at least 15 years prior to enrollment with a cumulative smoking history of <10 pack years. Patients will receive Iressa daily with the experimental cohort receiving ficlatuzumab at a dose of 20mg/kg on days 1 and 15 of a 28-day cycle. Crossover from Iressa monotherapy to ficlatuzumab combination therapy is allowed.

Stratification factors include ECOG performance status (0-1 or 2), smoking status (nonsmoker vs. light ex smoker) and gender. The study completed enrollment of 188 patients in 2011 and is expected to report top-line PFS data in 1H12 with full data presentation at a medical meeting in 2H12. In addition to clinical outcomes, biomarker data will explore:

- Tumor
    - EGFR mutation
    - C-Met, HGF and phospho-Met expression by immunohistochemistry (IHC)
    - C-Met gene copy number by FISH
    - Phospho-Akt, phosph S6, phospho- Erk and CD31 expression by IHC

- Serum
    - HGF, angiogenic and inflammatory markers

The most obvious competitor to ficlatuzumab is AMGN's AMG-102 also an antibody to HGF. Based on the clinicaltriasl.gov website, AMG-102 entered phase 2 development in renal cell carcinoma (RCC) and glioma in 2006. Since 2006, AMGN has listed 11 studies for AMG-102 on the clinicaltrials.gov web site enrolling more than 1,100 patients. In addition to the aforementioned tumors, AMGN has evaluated AMG-102 in ovarian, colorectal, gastric, prostate, mesothelioma and non small-cell lung cancers. In addition to monotherapy trials, AMGN has, or is, evaluating AM-102 with both targeted agents such as Avastin as well as with chemotherapy. Data from some of the randomized trials have been reported at medical meetings including castrate resistant prostate cancer (CRPC) where the addition of AMG-102 to mitoxantrone and prednisone did not increase overall survival compared to placebo. While some studies are ongoing including a single arm trial combining AMG-102 with Tarceva in NSCLC, in our opinion, AMGN's efforts to develop AMG-102 have yielded little in the way of positive data with little evidence that AMGN is willing to move AMG-102 into phase 3 testing.

Onartuzumab – A c-Met Antibody in Phase 3 Development

Roche's onartuzumab approaches inhibition of HGF from a different perspective by targeting the c-Met receptor as opposed to the ligand. Unlike AMGN, Roche has moved onartuzumab into a pivotal trial in Met over expressing NSCLC. Selected onartuzumab trials are summarized in Exhibit 23.

Exhibit 23: Selected Onartuzumab Trials

Sponsor	Drug	Class	Status	Trial Summary	2012 Milestone
Roche	Onartuxzumab MetMAB	Monoclonal c-MET	P3 2nd/3rd line Met +ve NSCLC - MetLUNG	480 pts Tarceva +/- metMAB. 1ary EP OS	Data 4Q15
			P2 1st line NSCLC	110 pts - Gem/cis +/- metMAB. 1ary EP PFS	Data 2Q14
			P2 1st line NSCLC	260 pts - chemo or chemo/Avastin +/- metMAB 1ary EP PFS	Data 4Q13
			P2 1st line Breast cancer	180 pts - paclitaxel +/-Avastin +/- metMAB 1ary EP PFS	Data 2Q14
			P2 1st line CRC	188 pts - FOLFOX/Avastin +/- metMAB 1ary EP PFS	Data 2Q14

Source: clinicaltrials.gov, ASCO and BMO Capital Markets

At the 2011 ASCO meeting, data for the phase 2 trial in NSCLC were presented. The trial enrolled 137 second/third line patients with tumor tissue available for biomarker analysis. Patients were randomized to Tarceva with onartuzumab (15mg/kg Q3wk) or placebo. Cross over was allowed in the placebo cohort and 27 patients crossed over to onartuzumab. The primary endpoint of the trial was PFS in the intention to treat cohort as well as a Met positive cohort. Met positivity was defined as a 2+ or 3+ score from an IHC assay. Ninety three percent of patients had adequate tissue for biomarker evaluation and of these 52% were deemed Met positive by IHC.

Baseline demographics included roughly two-thirds to one-third spilt between second and third line patients. The majority of patients had adenocarcinoma, with 29% having squamous histology. Both KRAS and EGFR mutation positive patients were well balanced between the

two arms at 23% and 12%, respectively. Based on Met over expression, an imbalance for squamous histology and smoking status was observed:

- 55-65% of Met +ve patients had adenocarcinoma versus 85% for Met negative patients
- 80% of Met +ve patients were smokers versus >90% for Met-ve.

Efficacy data from the ITT and Met expression stratified cohort are summarized in Exhibit 24.

Exhibit 24: Onartuzumab Phase 2 NSCLC Data

	ITT		Met+ve		Met-ve	
	Tarceva Placebo	Tarceva metMAB	Tarceva Placebo	Tarceva metMAB	Tarceva Placebo	Tarceva metMAB
PFS mo.	2.6	2.2	1.5	2.9	2.7	1.4
OS mo.	7.4	8.9	3.8	12.6	15.3	8.1

Source: ASCO 2011 and BMO Capital Markets

In the ITT population, the addition of onartuzumab was neither beneficial nor detrimental, however, in the Met +ve cohort, the addition of onartuzumab doubled PFS and tripled OS. In contrast, in the Met –ve cohort, the addition of onartuzumab decreased both PFS and OS by around 50%.

Further subsetting the Met +ve cohort by the presence or absence of Met gene amplification showed no difference between FISH +ve or FISH –ve, suggesting that Met gene dose is not a gating factor. KRAS mutation status is however, since there was no benefit for adding onartuzumab to the KRAS mutant population suggesting that KRAS status overrides Met status, however, given the small numbers of patients this observation will need to be validated in the ongoing phase 3 trial.

The effect of EGFR mutation status is unclear due to baseline imbalance. In the Met -ve cohort assigned to onartuzumab, no patients had mutated EGFR versus 14% for those assigned to placebo. In the met +ve cohort, the 8% of placebo and 23% of onartuzumab treated patients had a baseline EGFR mutation.

In addition to identifying a role of c-Met inhibition in met+ve NSCLC this trial also confirmed that Met +ve patients have a poor prognosis compared to Met –ve patients. In the placebo cohort the PFS and OS for met -ve patients was 2.7 and 15.3 months versus 1.5 and 3.8 months for the Met+ve cohort.

With respect to safety, the overall profile was dominated by Tarceva-related toxicity with the exception of a 23% vs. 6%-10% incidence of peripheral edema in the onartuzumab and placebo arms, respectively. The peripheral edema was noted to be generally low grade and reversible.

In a poster presented at ASCO on biomarkers, the authors note that a non-significant trend favoring onartuzumab was observed in patients with low baseline HGF versus those with high baseline HGF. No commentary on changes in HGF during onartuzumab therapy was observed.

Tivantinib – A c-Met TKI Antibody in Phase 3 Development

In addition to antibodies targeting HGF and c-Met there are several small molecules in development that target the Met signaling pathway. Pfizer's Xalkori was developed as Met inhibitor, but its ALK activity led to development and licensing in ALK +ve tumors. Exelixis's cabozanitib is also a Met pathway inhibitor, but based on unprecedented data in prostate cancer its assumed activity against other TKI's make it less of a competitor to ficlatuzumab, in our opinion. However, Arqule's tivantinib is a more specific inhibitor of the Met pathway and data in NSCLC has led to phase 3 trial initiation. The table in Exhibit 25 summarizes ongoing trial for tivantinib including two phase 3 trial in non-squamous NSCLC.

Exhibit 25: Selected Tivantinib Trials

Sponsor	Drug	Class	Status	Trial Summary	2012 Milestone
Arqule	Tivantinib	Small molecule	P3 2nd/3rd line NSCLC ex-Asia - MARQUEE	1000 pts Tarceva +/- 197. 1ary EP OS	CE and interim analysis
Daiichi	ARQ197		P3 2nd/3rd line NSCLC Asia - ATTENTION	470 pts Tarceva +/- 197. 1ary EP OS	
Sankyo			P2 HCC 2nd line	107 pts - 197 56% improvement in TTP vs placebo	Phase 1 Nexavar combo
			P2 CRC 2nf line KRAS WT	150 pts - Erbitux/irinotecan +/- 197	data
			P2 KRAS NSCLC	98 pts - Tarceva/197 vs chemotherapy	PFS data 2H12
			P2 Gastric 2nd/3rd line	30 pts single agent	PFS data 2Q/3Q12
			P2 Multiple myeloma -2-4th line	25 patients singel agent	ORR data 1Q/2Q12
			P2 Minimally/asymptomatic CRPC	78 patients single agent	ORR data 1Q/2Q12
					PFS data 1Q13

Source: clinicaltrials.gov and BMO Capital Markets.

At the 2011 ASCO meeting, data from a randomized phase 2 trial of tivantinib were presented as an oral late breaker. The trial randomized 167 second/third line NSCCL patients to Tarceva plus placebo or tivantinib 360mg/d. Crossover from placebo to tivantinib was allowed at progression and 23 of 83 placebo patients crossed over. The primary endpoint of the trial was investigator assessed PFS.

At baseline around 60% of patients had received one prior therapy, 30% had received two prior therapies, and the remainder had received more than two prior therapies, and all patients were EGFR inhibitor treatment naive. While all patients were required to have archival tissue for molecular analysis, EGF and KRAS mutation status could only be defined in around 70% of patients. Roughly 60% of patients were EGFR or KRAS wild type. While no imbalance for EGFR or KRAS wild type status was observed between the arms there was an imbalance for distribution of mutation +ve patients between the arms. In the tivantinib versus placebo arms, KRAS mutations were found in 12% vs. 6% of patients, however EGFR mutations were found in 7% and 13% of patients respectively.

The average duration of therapy was close to double in the tivantinib arm compared to placebo at 101 versus 65 days. The adverse event profile showed that tivantinib was well tolerated with no increase in grade 3 or 4 events and no statistically significant increase in grade 1 or 2 events, although an increase in vomiting from 13% in the placebo cohort to 25% in the tivantinib cohort was observed.

Exhibit 26: Tivantinib Phase 2 NSCLC Data

	ITT		Non-SCC	
	Tarceva Placebo	Tarceva T-nib	Tarceva Placebo	Tarceva T-nib
PFS wk.	9.7	16.1	9.7	18.9
OS wk.	29.4	36.6	29.4	43.1

Source: ASCO 2011 and BMO Capital Markets.

In the overall population a non-significant improvement in both PFS and OS was observed, however, in the non-squamous cell carcinoma subset of patients (n=117) a significant three-month improvement in overall survival was noted. Analysis of data by mutation status of KRAS and EGFR, suggests that patients with mutant KRAS benefited from tivantinib, but those with mutant EGFR did not; a trend favoring a tivantinib benefit was observed in patients with wild type EGFR. Met amplification status by FISH did not influence tivantinib efficacy

Following progress on the placebo arm, patients could cross over to tivantinib and 23 of 83 patients did so. Clinical benefit was observed in 11 patients including 2 who achieved a partial response (PR). Both patients were KRAS wild type and c-Met FISH positive, one patient was EGFR mutant positive and the other indeterminate.

C-Met Summary

The two agents ahead of ficlatuzumab suggest that for a subset of patients the combination of an EGF receptor tyrosine kinase inhibitor with a c-Met pathway inhibitor is effective. Comparing the onartuzumab and tivantinib trials, while acknowledging some differences in baseline demographics and small number of patients may suggest some differences between a small molecule versus an antibody approach.

In both trials no statistically significant differences in either PFS or OS were observed in the intent to treat populations, however, statistically significant differences were observed in subsets, namely the Met IHC subset in the onartuzumab trial and the non-squamous cell carcinoma subset in the tivantinib trial. Interestingly, histology did not seem to be a gating factor for response in the onartuzumab trial. With respect to the role of Met over-expression, ARQL has not reported data for Met IHC.

One interesting difference between the two agents is the effect of KRAS mutation status. With onartuzumab, KRAS overrides met such that met inhibition did not overcome the effect of KRAS. In the tivantinib trials however, met inhibition had a more significant impact on patients with KRAS mutations than those with wild type KRAS. There may also be slight differences in the tolerability profile as peripheral edema was noted only in the onartuzumab trial and an excess of vomiting in the tivantinib trial.

Obviously, ficlatuzumab development in NSCLC lags behind Roche's onartuzumab and ARQL's tivantinib. In addition, it may be instructive that AMGN's AMG-102 appears to be less effective than onartuzumab perhaps suggesting that targeting c-Met is preferable to targeting HGF in metastatic disease. While neither Roche nor ARQL have reported the effects

of their inhibitor on soluble HGF, AVEO has reported that HGF levels increase during ficlatuzumab therapy suggesting a compensatory mechanism of HGF blockade. Beyond NSCLC, it is also clear that both Roche and ARQL have broader development programs for their met inhibitors than NSCLC again putting AVEO at a disadvantage, in our opinion.

Other companies mentioned (priced as of the close on March 9, 2012):

ArQule (ARQL, $7.29, Not Rated)
Exelixis (EXEL, $5.26, Not Rated)
GlaxoSmithKline (GSK, $44.59, Not Rated)
Onyx Pharmaceuticals (ONXX, $38.14, **OUTPERFORM**)
Pfizer (PFE, $21.48, Not Rated)

Exhibit 27: AVEO Income Statement 2011A-2016E

INCOME STATEMENT ($M)	2011A	1Q12E	2Q12E	3Q12E	4Q12E	2012E	2013E	2014E	2015E	2016E
REVENUES										
Product Revenue	$ -	$ -	$ -	$ -	$ -	$ -	$ 9.3	$ 37.5	$ 66.7	$ 135.8
Collaboration Revenue	164.8	-	-			-	-	-	-	-
Other Revenue	-	-	-	20.0	10.0	30.0	60.0	24.5	24.5	-
TOTAL REVENUES	**$ 164.8**	$ -	$ -	$ 20.0	$ 10.0	**$ 30.0**	**$ 69.3**	**$ 62.0**	**$ 91.2**	**$ 135.8**
EXPENSES (GAAP)										
Cost of Goods Sold (COGS)	$ -	$ -	$ -	$ -	$ -	$ -	$ 0.9	$ 3.7	$ 6.7	$ 13.5
R&D Expense	101.7	25.0	30.0	35.0	40.0	130.0	140.0	140.0	130.0	120.0
SG&A Expense	29.2	7.0	7.0	7.0	7.0	28.0	28.0	28.1	28.0	28.0
Other Expenses	-	-	-	-	-	-	-	-	-	-
TOTAL EXPENSES	130.9	32.0	37.0	42.0	47.0	158.0	168.9	171.9	164.7	161.5
OPERATING INCOME (GAAP)	**33.9**	**(32.0)**	**(37.0)**	**(22.0)**	**(37.0)**	**(128.0)**	**(99.6)**	**(109.9)**	**(73.4)**	**(25.8)**
Depreciation and amortization	-	-	-	-	-	-	-	-	-	-
EBIT	33.9	(32.0)	(37.0)	(22.0)	(37.0)	(128.0)	(99.6)	(109.9)	(73.4)	(25.8)
Interest Income	0.5	0.2	0.1	0.1	0.1	0.5	0.4	0.3	0.7	0.7
Interest Expense	(3.8)	(0.8)	(0.8)	(0.8)	(0.8)	(3.2)	(3.2)	(3.0)	(3.0)	(3.0)
Other Income	0.0	-	-	-	-	-	-	-	-	-
Total Other Revenue (Expense)	(3.3)	(0.6)	(0.7)	(0.7)	(0.7)	(2.7)	(2.8)	(2.7)	(2.3)	(2.3)
Pre-Tax Income	30.6	(32.6)	(37.7)	(22.7)	(37.7)	(130.7)	(102.5)	(112.5)	(75.7)	(28.0)
Income Taxes	-	-	-	-	-	-	-	-	-	-
Net Income (Loss) (GAAP)	**$ 30.6**	**$ (32.6)**	**$ (37.7)**	**$ (22.7)**	**$ (37.7)**	**$ (130.7)**	**$ (102.5)**	**$ (112.5)**	**$ (75.7)**	**$ (28.0)**
Extraordinary item (net of taxes)	-	-	-	-	-	-	-	-	-	-
Reported Net Income (Loss) (GAAP)	$ 30.6	$ (32.6)	$ (37.7)	$ (22.7)	$ (37.7)	$ (130.7)	$ (102.5)	$ (112.5)	$ (75.7)	$ (28.0)
Reconciliation of Reported GAAP to Non-GAAP										
R&D Stock Compensation Expense	1.8	0.5	0.6	0.7	0.7	2.5	2.5	2.5	2.5	2.5
SG&A Stock Compensation Expense	2.5	0.8	0.8	0.8	0.8	3.2	3.2	3.2	3.2	3.2
Other Adjustments	-	-	-	-	-	-	-	24.5	24.5	-
Total of Reconciliation Items	4.3	1.3	1.4	1.5	1.5	5.7	5.7	30.2	30.2	5.7
Net Income (Non-GAAP)	$ 34.9	$ (31.3)	$ (36.3)	$ (21.2)	$ (36.2)	$ (125.0)	$ (96.8)	$ (82.3)	$ (45.5)	$ (22.3)
EPS (GAAP) (basic)	$ 0.77	$ (0.76)	$ (0.87)	$ (0.52)	$ (0.87)	$ (3.02)	$ (2.10)	$ (2.21)	$ (1.41)	$ (0.50)
EPS (GAAP) (diluted)	**$ 0.74**	**$ (0.76)**	**$ (0.87)**	**$ (0.52)**	**$ (0.87)**	**$ (3.02)**	**$ (2.10)**	**$ (2.21)**	**$ (1.41)**	**$ (0.50)**
Impact of Adjustments to EPS	0.11	0.03	0.03	0.03	0.03	0.13	0.12	0.59	0.56	0.10
EPS (Non-GAAP) (basic)	$ 0.88	$ (0.73)	$ (0.84)	$ (0.49)	$ (0.84)	$ (2.89)	$ (1.98)	$ (1.61)	$ (0.85)	$ (0.40)
EPS (Non-GAAP) (diluted)	$ 0.85	$ (0.73)	$ (0.84)	$ (0.49)	$ (0.84)	$ (2.89)	$ (1.98)	$ (1.61)	$ (0.85)	$ (0.40)
Weighted average shares outstanding - basic	39.7	43.2	43.2	43.3	43.3	43.2	48.9	51.1	53.8	56.2
Weighted average shares outstanding - diluted	41.5	43.2	43.2	43.3	43.3	43.2	48.9	51.1	53.8	56.2

Source: Company reports and BMO Capital Markets estimates.

Exhibit 28: AVEO Balance Sheet 2011A-2016E

BALANCE SHEET ($M)	2011A	1Q12E	2Q12E	3Q12E	2012E	2013E	2014E	2015E	2016E
Current Assets									
Cash and cash equivalents	$ 43.5	$ 35.3	$ 22.1	$ 3.8	$ 0.5	$ 60.8	$ 91.0	$ 78.0	$ 47.7
Short-term investments	177.6	152.6	127.6	127.6	127.6	27.6	27.6	27.6	27.6
Total cash, cash equivalents, and short-term investments	$ 221.1	$ 187.9	$ 149.7	$ 131.4	$ 128.1	$ 88.4	$ 118.6	$ 105.6	$ 75.3
Accounts receivable	7.2	7.2	7.2	7.2	7.2	7.2	7.2	7.2	7.2
Inventories	-	-	-	-	-	-	-	-	-
Prepaid expense and other current assets	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1
Total Current Assets	$ 234.4	$ 201.2	$ 163.0	$ 144.7	$ 141.4	$ 101.7	$ 131.9	$ 118.9	$ 88.6
Property and equipment, net	5.5	6.0	6.6	7.2	7.7	10.0	12.3	14.5	16.8
Restricted cash	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Marketable securities, non-current portion	54.3	54.3	54.3	54.3	54.3	54.3	54.3	54.3	54.3
Other assets	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
TOTAL ASSETS	$ 295.1	$ 262.4	$ 224.7	$ 207.0	$ 204.3	$ 166.9	$ 199.3	$ 188.6	$ 160.6
Current Liabilities									
Accounts payable	8.9	8.9	8.9	8.9	8.9	8.9	8.9	8.9	8.9
Accrued liabilities	14.3	14.3	14.3	14.3	14.3	14.3	14.3	14.3	14.3
Loans payable, net of discount	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6
Accrued compensation	-	-	-	-	-	-	-	-	-
Deferred revenue	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3
Other liabilities	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Liability for contingent consideration, current portion	-	-	-	-	-	-	-	-	-
Deferred rent	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Escrow account liability	-	-	-	-	-	-	-	-	-
Long-term debt, current portion	-	-	-	-	-	-	-	-	-
Total Current Liabilities	$ 34.6	$ 34.6	$ 34.6	$ 34.6	$ 34.6	$ 34.6	$ 34.6	$ 34.6	$ 34.6
Long-term debt, noncurrent portion	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6
Long-term deferred revenue	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7
Deferred rent	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Partnership liability							80.0	80.0	80.0
Liability for contingent consideration, non-current portion	-	-	-	-	-	-	-	-	-
Deferred tax liability	-	-	-	-	-	-	-	-	-
Advance from collaboration partner	-	-	-	-	-	-	-	-	-
Lease termination exit costs, non-current	-	-	-	-	-	-	-	-	-
Other liabilities	1.2	1.2	1.2	6.2	41.2	41.2	41.2	41.2	41.2
TOTAL LIABILITIES	$ 71.5	$ 71.5	$ 71.5	$ 76.5	$ 111.5	$ 111.5	$ 191.5	$ 191.5	$ 191.5
Shareholder's Equity									
Preferred stock	-	-	-	-	-	-	-	-	-
Common stock, at par	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Additional paid-in capital	429.5	429.5	429.5	429.5	429.5	494.5	559.5	624.5	624.5
Accumulated other comprehensive (loss) income	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)
Deferred compensation	-	-	-	-	-	-	-	-	-
Accumulated deficit	(205.9)	(238.5)	(276.2)	(298.9)	(336.6)	(439.1)	(551.6)	(627.3)	(655.3)
TOTAL SHAREHOLDER'S EQUITY (DEFICIT)	$ 223.5	$ 190.9	$ 153.2	$ 130.5	$ 92.8	$ 55.3	$ 7.8	$ (2.9)	$ (30.9)
TOTAL LIABILITIES AND SHAREHOLDER'S EQUITY	$ 295.1	$ 262.4	$ 224.7	$ 207.0	$ 204.3	$ 166.9	$ 199.3	$ 188.6	$ 160.6

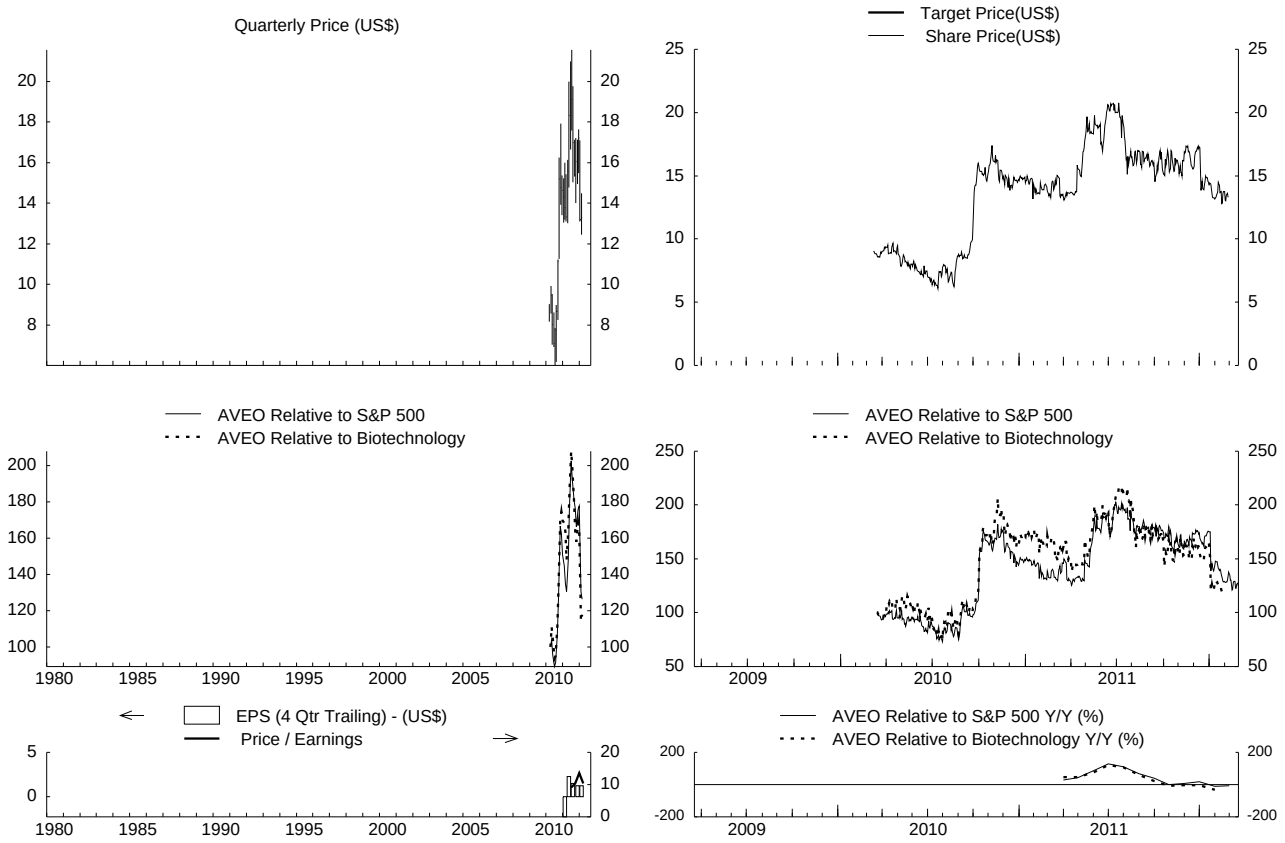
Source: Company reports and BMO Capital Markets estimates.

Exhibit 29: AVEO Statement of Cash Flows 2011A-2016E

CASH FLOW STATEMENT ($M)	2011E	1Q12E	2Q12E	3Q12E	2012E	2013E	2014E	2015E	2016E
Cash Flow From Operations									
Net Income	$ (25.2)	$ (32.6)	$ (37.7)	$ (22.7)	$ (37.7)	$ (13.6)	$ (25.7)	$ (17.0)	$ 0.8
Adjustments to reconcile net income to cash from operations									
Depreciation & amortization	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Stock-based compensation	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Non-cash interest expense	-	-	-	-	-	-	-	-	-
Deferred rent	-	-	-	-	-	-	-	-	-
Loss on disposal of property and equipment	-	-	-	-	-	-	-	-	-
Income from sale of assets to a related party	-	-	-	-	-	-	-	-	-
Restructuring and other	-	-	-	-	-	-	-	-	-
Excess tax benefit from stock-based awards	-	-	-	-	-	-	-	-	-
Forgiveness of notes receivable	-	-	-	-	-	-	-	-	-
Amortization of deferred compensation	-	-	-	-	-	-	-	-	-
Amortization of premium on investments	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-
Working Capital Adjustments									
Accounts receivable	2.5	-	-	-	-	-	-	-	-
Prepaid expenses and other current assets	-	-	-	-	-	-	-	-	-
Restricted cash	-	-	-	-	-	-	-	-	-
Other assets	(0.1)	-	-	-	-	-	-	-	-
Accounts payable	(0.8)	-	-	-	-	-	-	-	-
Accrued clinical trials and related expenses	2.4	-	-	-	-	-	-	-	-
Advance payable to collaboration partner	-	-	-	-	-	-	-	-	-
Accrued liabilities	-	-	-	-	-	-	-	-	-
Accrued compensation	-	-	-	-	-	-	-	-	-
Deferred rent	(0.0)	-	-	-	-	-	-	-	-
Deferred revenue	(0.3)	-	-	-	-	-	-	-	-
Lease termination exit costs liability	0.1	-	-	-	-	-	-	-	-
Other assets and liabilities, net	(1.7)	(1.7)	(1.7)	(1.7)	(1.7)	(1.7)	(1.7)	(1.7)	(1.7)
Total Working Capital Increase (Decrease)	$ 2.1	$ (1.7)	$ (1.7)	$ (1.7)	$ (1.7)	$ (1.7)	$ (1.7)	$ (1.7)	$ (1.7)
TOTAL CASH FROM OPERATIONS	**$ (21.0)**	**$ (32.2)**	**$ (37.2)**	**$ (22.3)**	**$ (37.3)**	**$ (13.1)**	**$ (25.3)**	**$ (16.5)**	**$ 1.2**
Cash From Investing Activities									
Purchases of marketable securities	-	-	-	-	-	-	-	-	-
Proceeds from maturities and sales of marketable securities	36.3	25.0	25.0	-	-	25.0	-	-	-
Maturities of short-term investments	-	-	-	5.0	35.0	-	-	-	-
Capital expenditures	(0.7)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)	(1.0)
Acquisition of Proteolix	-	-	-	-	-	-	-	-	-
Partnership							-	-	-
Notes receivable from related parties	-	-	-	-	-	-	-	-	-
Transfers (to)/from restricted cash	-	-	-	-	-	-	-	-	-
Payment for liability for contingent consideration	(17.0)	-	-	-	-	-	-	-	-
Proceeds from sale of fixed assets	-	-	-	-	-	-	-	-	-
TOTAL CASH FROM INVESTING	$ 18.6	$ 24.0	$ 24.0	$ 4.0	$ 34.0	$ 24.0	$ (1.0)	$ (1.0)	$ (1.0)
Cash From Financing Activities									
Borrowings under long-term debt	-	-	-	-	-	-	-	-	-
Debt issuance costs	-	-	-	-	-	-	-	-	-
Payments on long-term debt	(2.3)	-	-	-	-	-	-	-	-
Advance from (payment to) collaboration partner	-	-	-	-	-	-	-	-	-
Proceeds from exercise of stock options and issuance of common stock	-	-	-	-	-	-	-	-	-
Net proceeds from issuances of preferred stock	-	-	-	-	-	-	-	-	-
Proceeds from issuance of common stock, net of issuance costs	2.3	-	-	-	-	-	65.0	65.0	-
Repurchase of common stock	-	-	-	-	-	-	-	-	-
TOTAL CASH FROM FINANCING	$ 0.0	$ -	$ -	$ -	$ -	$ -	$ 65.0	$ 65.0	$ -
Increase (Decrease) in Cash and Cash Equivalents	**(2.4)**	**(8.2)**	**(13.2)**	**(18.3)**	**(3.3)**	**10.9**	**38.7**	**47.5**	**0.2**
Cash and cash equivalents at beginning of quarter	45.9	43.5	35.3	22.1	3.8	49.9	52.3	30.5	47.5
Cash and cash equivalents at end of quarter	**$ 43.5**	**$ 35.3**	**$ 22.1**	**$ 3.8**	**$ 0.5**	**$ 60.8**	**$ 91.0**	**$ 78.0**	**$ 47.7**

Source: Company reports and BMO Capital Markets estimates.

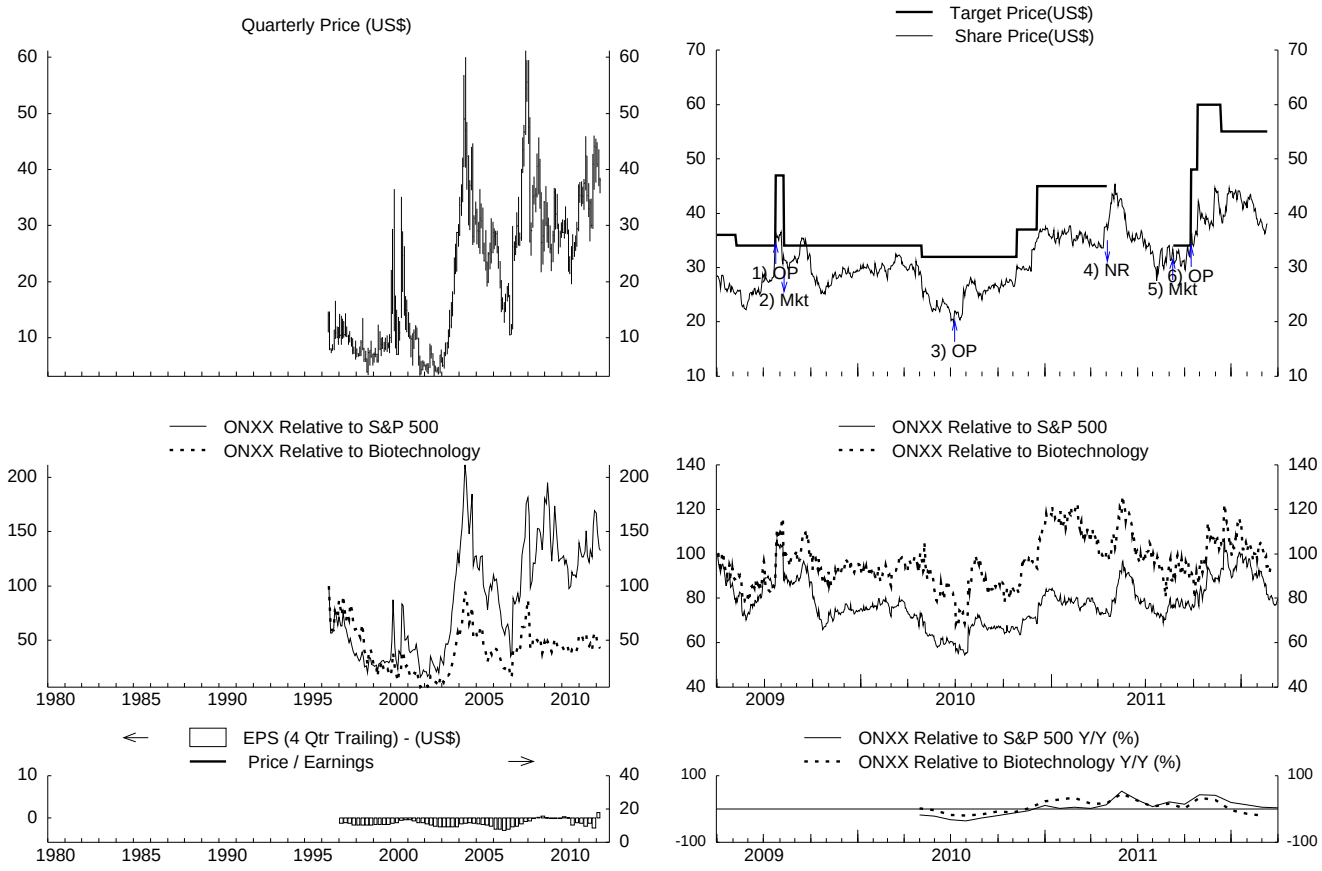
AVEO PHARMACEUTICALS INC (AVEO)



AVEO - Rating as of 30-Dec-11 = NR

Last Daily Data Point: February 27, 2012

ONYX PHARMACEUTICALS INC (ONXX)



ONXX - Rating as of 31-Mar-09 = Mkt

	Date	Rating Change	Share Price
1	23-Jul-09	Mkt to OP	$34.72
2	10-Aug-09	OP to Mkt	$32.21
3	8-Jul-10	Mkt to OP	$20.84
4	3-May-11	OP to NR	$38.00
5	7-Sep-11	NR to Mkt	$31.53
6	13-Oct-11	Mkt to OP	$34.49

Last Daily Data Point: March 9, 2012

Important Disclosures

Analyst's Certification

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Company Specific Disclosure for AVEO

Disclosure 9: BMO Capital Markets makes a market in this security.

Methodology and Risks to Our Price Target/Valuation

Methodology: Our $13 price target is based on 25x 2017E EPS of $1.00 discounted 20%..

Risks: There are a number of risks associated with investment in biotechnology companies. These risks include, but are not limited to, risk of clinical trial delay or failure, adverse regulatory decisions including product non-approval, unanticipated adverse effects of drugs which may result in removal from market, risk of manufacturing difficulties, capital market risk which may impair the ability to fund product discovery, research, regulatory filing, manufacture and/or commercialization, risk in attaining and retaining appropriate development or commercial partners, lower-than-expected product adoption, difficulties in gaining appropriate reimbursement for products from payors, unforeseen generic and branded competition, risk to patents being invalidated, and failure to meet earnings and revenue expectations.

Company Specific Disclosures for ONXX

9 - BMO Capital Markets makes a market in this security.

Methodology and Risks to Our Price Target/Valuation

Methodology: We arrive at our price target by applying a 25x multiple to 2015 non-GAAP EPS estimate of $3.30 and discounting at 20%. The higher multiple and lower discount rate reflects increased confidence in long-term estimates beyond 2015.

Risks: There are a number of risks associated with investment in biotechnology companies. These risks include, but are not limited to, risk of clinical trial delay or failure, adverse regulatory decisions including product non-approval, unanticipated adverse effects of drugs which may result in removal from market, risk of manufacturing difficulties, capital market risk which may impair the ability to fund product discovery, research, regulatory filing, manufacture and/or commercialization, risk in attaining and retaining appropriate development or commercial partners, lower-than-expected product adoption, difficulties in gaining appropriate reimbursement for products from payors, unforeseen generic and branded competition, risk to patents being invalidated, and failure to meet earnings and revenue expectations.

Risks particular to ONXX include, but are not limited to, inability to grow Nexavar further in HCC, increased erosion of Nexavar base in RCC, demonstration of superiority to Nexavar by competitors in RCC and HCC, failure to succeed in label expansion studies, including MISSION study in NSCLC, failure to gain accelerated approval for carfilzomib in myeloma and failure to demonstrated a survival benefit for carfilzomib in larger phase 3 trials.

Distribution of Ratings (December 30, 2011)

Rating Category	BMO Rating	BMOCM US Universe*	BMOCM US IB Clients**	BMOCM US IB Clients***	BMOCM Universe****	BMOCM IB Clients*****	Starmine Universe
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Hold	Market Perform	60.3%	9.6%	59.6%	56.3%	52.2%	39.4%
Sell	Underperform	1.7%	0.0%	0.0%	3.0%	1.6%	4.4%

* Reflects rating distribution of all companies covered by BMO Capital Markets Corp. equity research analysts.

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Und = Underperform - Forecast to underperform the market;
(S) = speculative investment;
NR = No rating at this time;

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