Karyopharm Therapeutics Inc. (KPTI)

Encouraging Solid Tumor Updates at ESMO

MARKET OUTPERFORM | Price: $42.10 | Target Price: $50.00

MARKET DATA

Price	$42.10
52-Week Range:	$15.50 - $47.98
Shares Out. (M):	32.6
Market Cap ($M):	$1,372.5
Average Daily Vol. (000):	85.0
Cash (M):	$226
Cash/Share:	$6.93
Enterprise Value (M):	$1,041
Float (M):	14.6
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2013A	2014E	2015E
Revenue ($M)	1Q	--	$0.2A	$0.0
	2Q	$0.4	$0.0A	$0.0
	3Q	$0.0	$0.0	$0.0
	4Q	$0.0	$0.0	$0.0
	FY	**$0.0**	**$0.0**	**$0.0**
EPS	1Q	--	($0.46)A	--
	2Q	($5.39)	($0.55)A	--
	3Q	($3.66)	($0.58)	--
	4Q	($0.47)	($0.63)	--
	FY	**($5.59)**	**($2.20)**	**($4.75)**

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

INVESTMENT HIGHLIGHTS

Phase I updates at ESMO in prostate, head and neck, and ovarian cancer highlight the durability of disease stabilization in heavily refractory populations; reiterate our Market Outperform and $50 price target. KPTI presented updates from three cohorts of the solid tumor Phase I study with selinexor at ESMO over the weekend and today. In prostate cancer, stable disease was achieved in 9/11 evaluable patients, in some patients lasting up to ~300-400 days. We were also encouraged by head and neck results, where data show durations of stable disease and TTP that meet or exceed those of the prior therapy. Together, we believe these data continue to demonstrate Selinexor monotherapeutic activity in solid tumors. We note that several company and investigator-sponsored studies are currently ongoing in each of CRPC, squamous cell carcinomas (the STARRS trial), and gynecologic cancers (the SIGN trial), in order to inform the best path(s) forward in solid tumors. We derive our $50 price target based on the synthesis of our DCF and SOTP valuation methodologies.

Selinexor's durability of disease stabilization in CRPC is impressive, in our view, particularly in the context of a heavily pretreated patient group. Recall at ASCO, KPTI presented 7 of 8 evaluable SD events (ranging 114 to +300 days). With three additional patients on study since then, clinical activity reported today at ESMO was largely in line, including 9 of 11 SD events (ranging 69 – 430+ days, with three patients still on study). We note that evaluated patients were heavily pretreated, having seen a median of four prior therapies, including Xtandi (enzalutamide, 53% of enrolled), Zytiga (abiraterone, 53%), and docetaxel (100%). For five of the nine patients with SD, duration of therapy or time to progression (TTP) was similar to or exceeded TTP achieved by the most recent prior therapy (Figure 2). We believe these results speak favorably to Selinexor's differentiated (androgen-independent) mechanism of action, particularly in light of data suggesting diminished efficacy from successive AR-mediated therapy and with docetaxel in the post-abi/enzi setting.

Open Phase II studies in both the pre- and post-chemo settings will determine the path forward. Looking beyond the Phase I data today, we note that two single-arm Phase II trials in metastatic CPRC areunderway: 1) a 50-patient, company- sponsored trial in patients following treatment with enzalutamide (enz) and/or abiraterone (abi), unselective for prior chemotherapy; and 2) a 54-patient, investigator-sponsored study at UCSF in patients following treatment with enz and/or abi but before docetaxel or other chemotherapy. In our view, data from either of these trials (read-outs from KPTI likely at ASCO 2015) should paint a clearer picture of the potential efficacy and safety profile in the indication. We further believe that the approval of the IST protocol in the pre-chemo setting speaks to the perception of ongoing unmet need and to the strength of Selinexor data shown to date.

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Encouraging updates in squamous head and neck and ovarian cancer cohorts. Data from the HNSCC cohort overall were largely in line with that presented at ASCO (11/16 pts evaluable with SD compared to 9/14 SD, previously). Here again, we were impressed by the duration on study/TTP of many of the patients achieving SD, which, in most cases, exceeded TTP achieved by the most recent prior therapy. We view these results as all the more impressive, coming from a notoriously difficult disease and patient population.

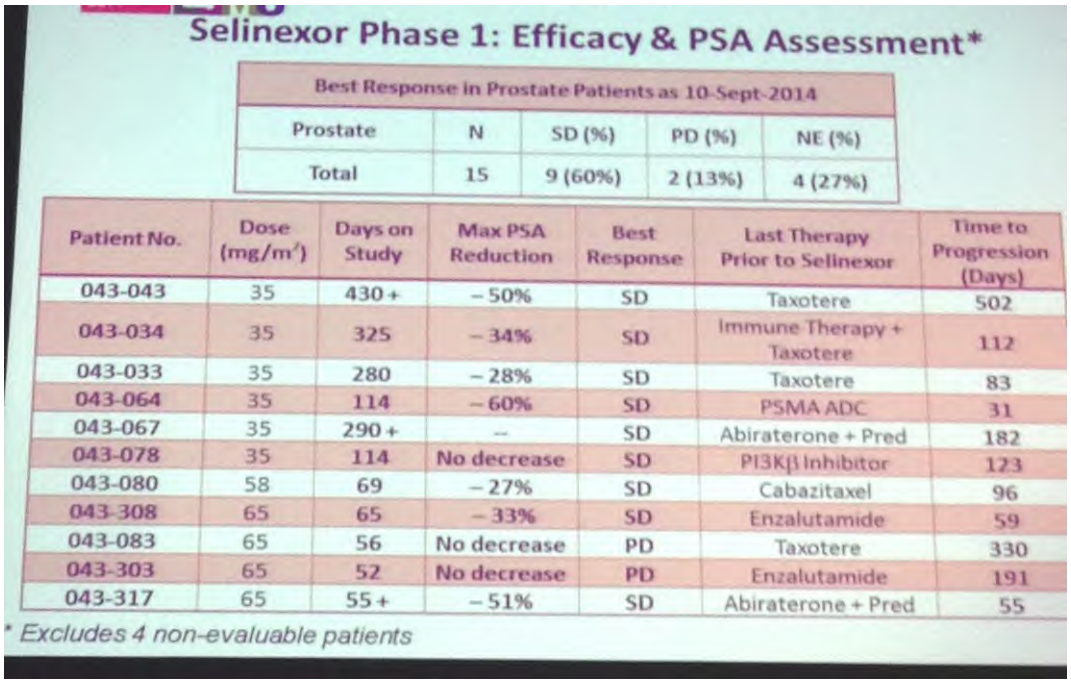
We remain encouraged by the signs of selinexor activity across a wide range of tumor types, both solid and liquid, exemplified by data presented at ASCO and EHA. We believe Karyopharm is on the verge of bringing an entirely new class of chemotherapy agent to the market with broad activity and acceptable tolerability. We remind the reader that Karyopharm holds the worldwide rights to Selinexor.

FIGURE 1. Upcoming Catalysts

Timing	Drug	Catalyst
4Q14	Selinexor	Initiation of second pivotal Phase II/III study in (3L+ DLBCL; SADAL)
4Q14	Selinexor	Initiation of Phase II in Richter's syndrome (SIRRT)
ASH	Selinexor	Updated RR/MM Phase I data in combination with dexamethasone
2H14	KPT-350	IND completion for use in inflammation, auto-immune, and anti-viral indications
2H14	PAK Inhibitor	IND completion for use in oncology indications

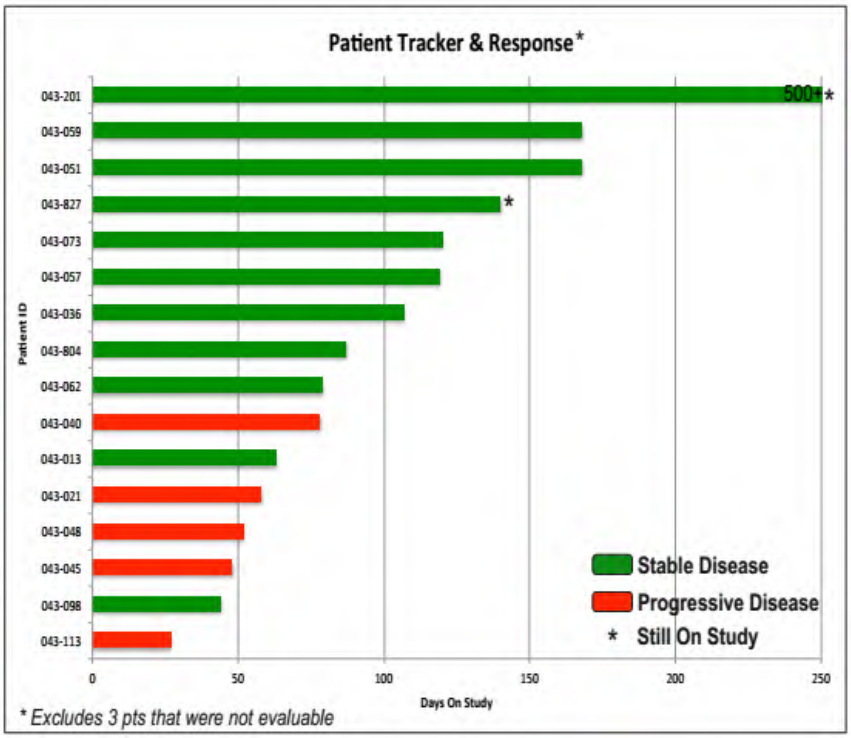
Source: Company presentations

FIGURE 2. Selinexor Phase I Activity in CRPC Cohort



Source: ESMO 2014

FIGURE 3. Duration on Study Among Head and Neck Squamous Patients Treated with Selinexor



Prior Therapies for Patients on Selinexor > 3 Months

Patient No.	Dose (mg/m^2)	Days on Study	Best Response	Last Therapy Prior to Selinexor	Time to Progression (Days)
043-201	35	>500	SD	Gemcitabine, Capecitabine	99
043-059	20	168	SD	Gemcitabine	49
043-051	35	168	SD	mTor Inhibitor	56
043-827	65	>140	SD	Gemcitabine, Capecitabine	118
043-073	35	120	SD	Carboplatin, Taxol	153
043-057	35	119	SD	Cetuximab	unknown
043-036	35	107	SD	Cetuximab, Carboplatin, Cisplatin, 5FU	118

Source: ESMO 2014

FIGURE 4. Selinexor Clinical Trials

Trial No.	Sponsor	Phase	Indication	Combo Partner	Pt Size	FPI
NCT01607892	KPTI	I	Various Heme Malignancies (MAD)		250	May-12
NCT01607905	KPTI	I	Various advance solid tumors		90	May-12
NCT02146833	KPTI	II	Metastatic prostate cancer (pre and post chemo eligible)		50	May-14
TBD	KPTI	II	**SADAL** - ≥3L R/R DLBLC, low and hi dose Selinexor		200	4Q14
NCT02088541	KPTI	II	**SOPRA** - R/R Elderly AML vs physician's choice		150	Apr-14
NCT02138786	KPTI	II	**SIRRT** - R/R Richter's Transformation		50	4Q14
NCT02025985	KPTI	II	**SIGN** - Gynaecologic malignancies (ovarian, endometrial, cervical)		63	Apr-14
NCT01986348	KPTI	II	**KING** - Glioblastoma		30	Mar-14
NCT02213133	KPTI	II	**STARRS** - R/R Squamous Cell Carcinomas (H&N, Lung, Esophagus)		66	Sep-14
NCT02178436	KPTI	I/II	Pancreatic cancer and PDAC	Gem/Abraxane	43	Not yet recruiting
NCT01896505	KPTI	I	Food effect study		20	Sep-13
NCT02215161	UCSF	II	pre-chemo mCRPC		54	Not yet recruiting
NCT02186834	Moffit	I/II	Multiple myeloma	Dexamethasone, Doxil	47	Not yet recruiting
NCT02199665	U. Chicago, NCI	I	Refractory Multiple Myeloma	Kyprolis, Dexamethasone	48	Not yet recruiting
NCT02093403	Ohio State	I	R/R and Elderly Untreated AML	Dacogen	42	Mar-14
NCT02120222	Ohio State	I	Recurrent melanoma		20	Not yet recruiting
NCT02137356	Sheba Med Ctr	I	Neoadjuvant rectal neoplasms	Chemoradiation	28	Not yet recruiting
NCT02069730	U of T		Salivary gland cancers		30	Not yet recruiting
NCT02091245	Dana Farber	I	Childhood relapsed ALL/AML		28	Apr-14
NCT02078349	Ntl Univ. Hosp, Singapore	I	Asian solid tumor study		30	Mar-14
NCT02228525	MSKCC	II	2L Myelodysplastic Syndrome (post-HMA)		20	Aug-14

Source: Clinicaltrials.gov

Company Description

Karyopharm Therapeutics (KPTI) is a Natick, MA-based, clinical-stage biopharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitors of Nuclear Export (SINE) compounds function by preventing the export of tumor suppressor proteins from the nucleus, driving accumulation and restoration of function. The company's lead pipeline candidate, selinexor (KPT-330), is a Phase I orally available small molecule inhibitor of XPO1, set to initiate pivotal Phase II/III evaluation in various hematologic malignancies in 2014. Karyopharm is also developing selinexor and SINE as potential therapies for autoimmune and inflammatory disease, viral infections, and wound healing.

Investment Risks

Clinical. Drug development is an inherently risky business. Clinical trials always carry a risk of failure and Karyopharm's assets (Selinexor (KPT330), KPT-350, PAK4 inhibitor, verdinexor or future drug candidates) may fail to demonstrate meaningful enough levels of efficacy in current or future clinical trials.

Regulatory and commercial. The ability of Karyopharm to market its drugs depends upon the drugs obtaining approval from the FDA and foreign regulatory agencies. Failure to achieve approval or delays in the timelines to approval could negatively impact the company's share price.

Competitive. Hematologic malignancies, including multiple myeloma, indolent non-Hodgkin lymphoma, and acute myeloid leukemia represent increasingly competitive fields and Karyopharm faces competition from both commercial and development-stage companies with product(s) or product candidates addressing similar clinical indications. Some of these companies may possess substantially greater R&D and commercial resources than Karyopharm. As such, there is no assurance Karyopharm will be competitive or differentiated from other drug products.

Financial. Following its IPO, Karyopharm ended 1Q14 with approximately $156MM in cash and cash equivalents. We anticipate the company is likely to seek additional equity financing in the form of a secondary offering in order to complete the development of its drug candidates, creating dilution risk for existing shareholders.

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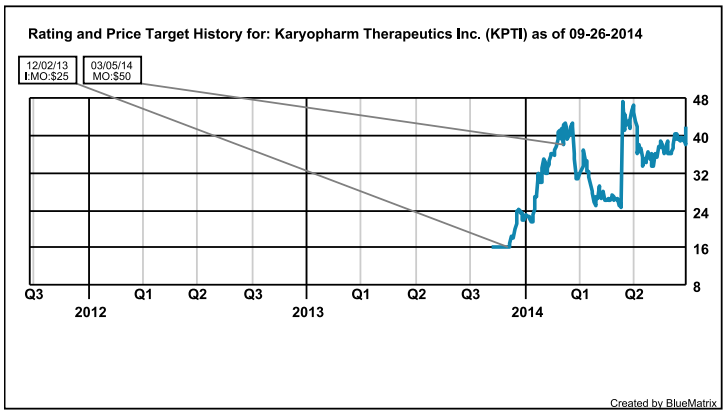
JMP Rating	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	# Co's Receiving IB Services in Past 12 Months	*% of Co's With This Rating*
MARKET OUTPERFORM	Buy	274	*60.62%*	Buy	274	*60.62%*	100	*36.50%*
MARKET PERFORM	Hold	139	*30.75%*	Hold	139	*30.75%*	19	*13.67%*
MARKET UNDERPERFORM	Sell	3	*0.66%*	Sell	3	*0.66%*	0	*0%*
COVERAGE IN TRANSITION		36	*7.96%*		36	*7.96%*	0	*0%*
TOTAL:		452	*100%*		452	*100%*	119	*26.33%*

Stock Price Chart of Rating and Target Price Changes:

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.



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