Karyopharm Therapeutics Inc. (KPTI)

First Glance at Promising Myeloma and NHL Data in ASH Abstracts

MARKET OUTPERFORM | Price: $41.73 | Target Price: $50.00

MARKET DATA

Price	$41.73
52-Week Range:	$15.50 - $47.98
Shares Out. (M):	32.6
Market Cap ($M):	$1,360.4
Average Daily Vol. (000):	304.0
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

ASH abstract data provides initial look into activity and Phase II dose of Karyopharm selinexor in relapsed/refractory NHL and confirms activity and dose in multiple myeloma; reiterate our Market Outperform rating and $50 price target based on DCF, CAGR, and SOTP methodologies. ASH abstracts became available online this morning. A total of ten abstracts are devoted to selinexor, two of which, we believe, significantly de-risk the clinical development path for the drug in two of its biggest potential indications (as a % of NPV), relapsed/refractory non-Hodgkin lymphoma (NHL) and relapsed/refractory multiple myeloma.

Robust activity seen with selinexor in R/R NHL, the likes of which have rarely been seen in this patient population. Following previous data from smaller studies in heavily pretreated patients, a total of 58 patients with a median of three prior regimens were treated with 13 doses that ranged from as low as 3mg/m2 to as high as 80mg/m2. Objective responses were seen across all NHL subtypes, and an objective response rate was seen in 31% of patients. A more impressive 40% ORR was seen in patients who received doses above 60mg/m2 and were diagnosed with R/R aggressive NHL, including DLBCL, follicular HNL, and transformed NHL (Richter's transformation). A total of five complete responses (CRs) were seen, four in DLBCL and one in T cell NHL. Lower doses saw correspondingly lower responses. The recommended Phase II dose is 60mg/m2. The typical selinexor side effects of nausea, anorexia, and thrombocytopenia were seen but are manageable with supportive care and dose reduction/interruption. Approximately 25% of patients have been able to remain on study for 6-23 months. In our view, these results bode well for the SADAL trial, the registration trial for selinexor in NHL, which is now entering its activation stage (see below for additional detail).

Follow-up data in myeloma shows continued favorable drug profile, RP2D is set. Recall that selinexor showed remarkable activity data at the EHA meeting in June in combination with low doses of dexamethasone (see our June 14, 2014 note). In a total of eight patients, responses were seen in four (ORR 50%), including one stringent complete response (sCR), while 6/8 (75%) patients achieved clinical benefit (CR+PR +MR+SD). A total of 28 patients with a median of six prior regimens, all of whom had received both an ImID (Revlimid) and a proteasome inhibitor (Velcade, Kyprolis), with more than two-thirds having received Pomalyst and/or Kyprolis (36%), attesting to the late-stage nature of the population. In contrast to the eight patients in the EHA dataset, a total of 10 patients were treated at 45mg/m2 twice weekly, along with 20mg of dexamethasone and experienced at 60% ORR with the same sCR seen in EHA, along with five PRs and a clinical benefit rate of 80%. The company's next steps are to move forward in Phase II studies with the combination of selinexor 45mg/m2 plus dexamethasone.

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Excerpts from our note on 2Q14 Earnings concerning DLBCL and multiple myeloma:

- **Feedback from FDA support accelerated path forward in R/R DLBCL on updated Phase II protocol design.** As noted on the call and in this morning's press release, the SADAL protocol has been modified to a two-arm, 1:1 randomized Phase IIb trial, evaluating high dose (flat dose of 100mg = 60mg/2) and low dose (50mg = 35mg/m2) Selinexor plus dexamethasone in 200 patients with ≥3L disease, maintaining ORR and duration of response as the basis for potential accelerated approval. Based on the relatively greater unmet need, the trial will target at least fifty percent enrollment of patients with GCB subtype disease. Based on positive feedback from EMA indicating the potential for registration using the modified protocol, SADAL will recruit from both in the U.S. and EU, beginning in 4Q14. Confirmatory studies in DLBCL could take the shape randomized trials in earlier line patients, evaluating standard of care (Rituximab chemoimmunotherpy) with and without Selinexor. A Phase I trial of Selinexor plus Rituximab in aggressive NHL is currently underway.

- **Encouraging myeloma activity in combination low-dose dex, the key study to watch in 2H14**. Recall that in Phase I data presented at EHA, selinexor in combination with low-dose dexamethasone showed a surprising 50% response rated in eight heavily pretreated myeloma patients (clinical benefit rate of 75%), vastly improving over single-digit response rates observed as a single agent. A majority of responding patients reportedly remain on study, while two target patients have been enrolled onto the combination expansion cohort. Abstracts submitted to EMSO could offer the opportunity for increased visibility on duration of response, although we suspect it won't be until ASH that we learn whether the combination is more broadly active. Assuming the data support an accelerated path forward for selinexor/dex in later-line MM, forthcoming ISTs evaluating selinexor plus standard myeloma therapies (e.g., Kyprolis) should confer solid positioning with respect to confirmatory trial design.

We remain encouraged by the signs of Selinexor activity across a wide range of tumor types, both solid and liquid, exemplified by the 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 also note that Karyopharm holds the worldwide rights to selinexor.

FIGURE 1. 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		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
NCT02178436	KPTI	I/II	Pancreatic cancer and PDAC	Gem/Abraxane	43	Not yet recruiting
NCT01896505	KPTI	I	Food effect study		20	Sep-13
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

Source: Company reports

FIGURE 2. Upcoming Milestones

Timing	Drug	Catalyst
ESMO	Selinexor	Updated Phase I presentations in solid tumor
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 RRMM 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 reports

FIGURE 3. KPTI Income Statement

Karyopharm Therapeutics (KPTI)	2011A	2012A	1Q14A	2Q14A	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Income Statement ($MM)	**2011A**	**2012A**	**1Q14A**	**2Q14A**	**3Q14E**	**4Q14E**	**2014E**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**
Product Sales and Royalties:																		
Selinexor																		
US Sales								-	44.1	103.6	308.1	842.2	1,463.8	2,093.2	2,649.0	3,094.2	3,434.0	3,577.8
ROW Royalties								-	-	6.8	17.1	43.2	111.9	209.3	285.6	359.0	436.2	470.0
Total Product Sales and Royalties	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	44.1	110.4	325.2	885.3	1,575.8	2,302.5	2,934.6	3,453.2	3,870.3	4,047.8
Collaboration Revenue	0.2	0.6																
Contract and grant revenue			0.2	0.0														
Total Revenue	0.2	0.6	0.2	0.0	0.0	0.0	0.0	0.0	44.1	110.4	325.2	885.3	1,575.8	2,302.5	2,934.6	3,453.2	3,870.3	4,047.8
Cost of Goods Sold									4.4	9.3	24.6	67.4	117.1	167.5	211.9	247.5	274.7	286.2
Gross Profit	0.2	0.6	0.2	0.0	0.0	0.0	0.2	0.0	39.7	101.1	300.5	818.0	1,458.7	2,135.0	2,722.7	3,205.6	3,595.6	3,761.6
Operating Expenses:																		
Research and Development	8.6	14.1	11.0	13.2	10.6	11.7	46.4	83.6	133.7	180.6	202.2	218.4	229.3	240.8	252.8	265.5	286.7	301.0
General and administrative	1.8	2.4	2.9	3.3	2.9	4.0	13.1	78.7	114.1	139.8	160.7	176.8	194.5	210.0	226.8	245.0	264.6	277.8
Total operating expenses	10.5	16.5	13.9	16.5	13.5	15.7	59.6	162.3	247.8	320.3	362.9	395.2	423.8	450.8	479.7	510.4	551.3	578.8
Operating income (loss)	(10.3)	(15.9)	(13.7)	(16.5)	(13.5)	(15.7)	(59.4)	(162.3)	(208.1)	(219.2)	(62.4)	422.8	1,034.9	1,684.2	2,243.0	2,695.2	3,044.3	3,182.7
Other income (expense):																		
Interest income	0.0	0.0	0.0	0.0														
Interest expense	0.0	0.0																
Total other income, net	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Change in fair value of preferred stock warrant liability	0.0	0.0																
Foreign currency transaction gain (loss)	0.0	0.0																
Pretax income (loss)	(10.3)	(15.9)	(13.7)	(16.5)	(13.5)	(15.7)	(59.3)	(162.3)	(208.1)	(219.2)	(62.4)	422.8	1,034.9	1,684.2	2,243.0	2,695.2	3,044.3	3,182.7
Income tax benefit (provision)							0.0	0.0	0.0	0.0	0.0	0.0	(155.2)	(336.8)	(560.8)	(808.6)	(1,065.5)	(1,114.0)
Tax Rate							*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*15%*	*20%*	*25%*	*30%*	*35%*	*35%*
Comprehensive income (loss)	(10.3)	(15.9)	(13.7)	(16.5)	(13.5)	(15.7)	(59.3)	(162.3)	(208.1)	(219.2)	(62.4)	422.8	879.6	1,347.4	1,682.3	1,886.6	1,978.8	2,068.8
Accretion of redeemable convertible preferred stock	0.0	0.0																
Net income (loss) attributable to common stockholders	(10.3)	(15.9)	(13.7)	(16.5)	(13.5)	(15.7)	(59.3)	(162.3)	(208.1)	(219.2)	(62.4)	422.8	879.6	1,347.4	1,682.3	1,886.6	1,978.8	2,068.8
Basic EPS to common shareholders	$ (10.27)	$ (8.95)	$ (0.46)	$ (0.55)	$ (0.47)	$ (0.55)	$ (2.06)	$ (5.63)	$ (6.79)	$ (6.75)	$ (1.91)	$ 12.93	$ 26.81	$ 40.93	$ 50.93	$ 56.93	$ 59.52	$ 62.02
Diluted EPS to common shareholders	$ (10.27)	$ (8.95)	$ (0.46)	$ (0.55)	$ (0.47)	$ (0.55)	$ (2.06)	$ (5.63)	$ (6.79)	$ (6.75)	$ (1.91)	$ 12.56	$ 26.05	$ 39.78	$ 49.50	$ 55.33	$ 57.84	$ 60.27
Basic shares outstanding	1.0	1.8	29.6	29.7	28.8	28.8	28.8	28.8	30.6	32.5	32.6	32.7	32.8	32.9	33.0	33.1	33.2	33.4
Diluted shares outstanding	1.0	1.8	29.6	28.8	28.8	28.8	28.8	28.8	30.6	32.5	32.6	33.7	33.8	33.9	34.0	34.1	34.2	34.3

Source: JMP Securities LLC, Company reports

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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Market Outperform (MO): JMP Securities expects the stock price to outperform relevant market indices over the next 12 months.
Market Perform (MP): JMP Securities expects the stock price to perform in line with relevant market indices over the next 12 months.
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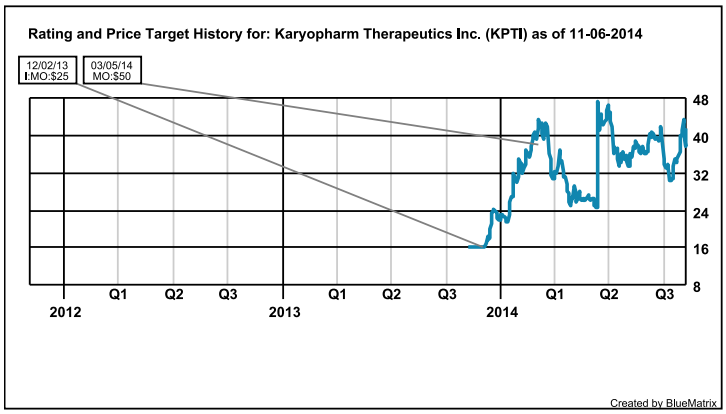
MARKET OUTPERFORM	Buy	286	*61.37%*	Buy	286	*61.37%*	105	*36.71%*
MARKET PERFORM	Hold	140	*30.04%*	Hold	140	*30.04%*	15	*10.71%*
MARKET UNDERPERFORM	Sell	2	*0.43%*	Sell	2	*0.43%*	0	*0%*
COVERAGE IN TRANSITION		36	*7.73%*		36	*7.73%*	0	*0%*
TOTAL:		466	*100%*		466	*100%*	122	*26.18%*

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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