September 29, 2014

HEALTHCARE/BIOTECHNOLOGY

Karyopharm Therapeutics

ESMO Prostate Data Look Just OK; Ovarian, H&N Updates Offer Little New

Stock Rating:

PERFORM

12-18 mo. Price Target	NA
KPTI - NASDAQ	$42.10
3-5 Yr. EPS Gr. Rate	NM
52-Wk Range	$47.98-$15.50
Shares Outstanding	29.8M
Float	8.4M
Market Capitalization	$1,375.4M
Avg. Daily Trading Volume	271,148
Dividend/Div Yield	NA/NM
Book Value	$4.87
Fiscal Year Ends	Dec
2014E ROE	NM
LT Debt	NA
Preferred	NA
Common Equity	$144M
Convertible Available	No

EPS Diluted	Q1	Q2	Q3	Q4	Year	Mult.
2013A	(2.52)	(2.97)	(3.66)	(2.00)	(5.59)	NM
2014E	(0.46)A	(0.55)A	(0.52)	(0.57)	(2.11)	NM
2015E	--	--	--	--	(2.52)	NM

Reflects 1:3.3 reverse stock split effective October 2013.

Revenue ($/mil)	Q1	Q2	Q3	Q4	Year	Mult.
2013A	0.2	0.1	0.0	0.0	0.4	NM
2014E	0.2A	0.0A	0.2	0.2	0.6	NM
2015E	--	--	--	--	2.0	NM

Yigal Nochomovitz, Ph.D.
212 667-8163
Yigal.Nochomovitz@opco.com

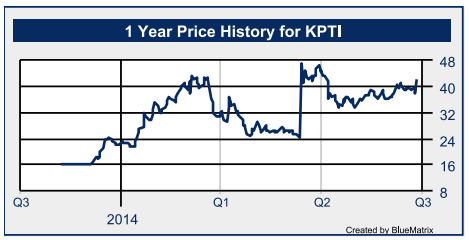
SUMMARY

Karyopharm presented Ph. 1 clinical updates in head & neck and ovarian cancer over the weekend at ESMO. Duration and response updates relative to ASCO 2014 were minimal (we do not model these indications). KPTI also posted slides on its site ahead of today's oral presentation for an ongoing Ph. 1 in prostate, the solid tumor apparently drawing significant attention from investors. For prostate, the best response of 9 stable diseases (60%) looks reasonable in a heavily pre-treated population, but we suspect this is somewhat below investors' expectations for the data. While interesting, we do not believe the prostate results are differentiated enough relative to historical data for patients refractory to novel mechanisms (i.e., Xtandi).

KEY POINTS

- **Prostate.** Median time to progression (TTP, 11 evaluable) now ~112 days vs. ~275 days (ASCO) given three new evaluable patients with an average TTP of ~100 days and two previously censored patients now progressing (average TTP ~150 days). There appears to be no dose response (the two PDs occurred at the higher 65 mg/m2).
- **Comps for Xtandi failures.** Studies testing Zytiga yielded PFS of 2.7-4 months with 1 PR (Ex. 1) in patients with ≥2 prior lines. The Selinexor data in patients with 4 prior lines (and SD as best response) appear in-line to possibly marginally better (worse patients) but seem to fall shy of being clearly differentiated.
- **Ovarian.** The only change relative to ASCO is the extension on days on study (320+ to 386) for one SD. A look at historical PFS in pt-refractory ovarian (Ex. 2) suggests patients with 4-5 prior lines achieve 4-4.5 months PFS and Selinexor's ~120 days among five evaluable (4.4 mean prior lines) does not stand out.
- **Head & Neck.** Two patients remain on study (vs. 4 at ASCO) and duration for the 2 remaining extending from >410 to 500+ days and 50 to 140 days. However, the median PFS of ~90 days appears underwhelming relative to afatinib (16 weeks) or chemotherapy (3.3 months for platinum + 5-FU).
- **Our focus remains on heme.** We model AML, DLBCL and myeloma where we see the best early data so far. The stock could see some pressure today given modest prostate results and in light of raised expectations.

Stock Price Performance



Company Description

Karyopharm Therapeutics is a clinical-stage biotechnology company focused on discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of blood cancers and solid tumors.

Exhibit 1

Historical Comps for Xtandi Failures

Patients	Age	# of Prior Therapies	# of Patients	Drug	Control	PFS	p value and/or 95% CI
mCRPC post-docetaxel and enzalutamide	71	2	38	Abiraterone/ Prednisone	Prednisone	2.7	2.3-4.1
mCRPC post docetaxel and enzalutamide	70*	≥2	30	Abiraterone/ Prednisone	Prednisone	Median PSA progression-free survival 15.4 weeks	10.7-20.2

* Age >70 years was associated with a worse PFS (14.6 weeks, (95% CI: 7.6-21.5) vs. 18 weeks (95% CI: 7.4-28.6) for patients ≤ 70 years (p=0.041)

Sources: Loriot, Y., et al. Ann Oncol. 2013, 24(7):1807-12; Noonan, K.L., et al. Ann. Oncol. 2013, 24 (7) 1802-1807.

Exhibit 2

Historical PFS in Platinum-Refractory Ovarian Cancer

# of Lines of Therapy	Progression Free Survival (95% Confidence Interval)
1	10.2 (9.6-10.7)
2	6.4 (5.9-7.0)
3	5.6 (4.8-6.2)
4	4.4 (3.7-4.9)
5	4.1 (3.0-5.1)

Sources: Hanker, L.C., et al. Ann Oncol 2012, 00:1-8.

Investment Thesis

We believe Karyopharm shares are currently fairly valued. The emerging Phase 1 data for Karyopharm's lead drug Selinexor suggest to us fair-to-good chances of approval as a salvage therapy in several advanced cancers. We focus our work on myeloma, DLBCL, elderly AML and sarcoma, where we currently see the strongest efficacy data and where modest share and duration assumptions in the relapsed/ refractory setting support the current valuation. We see room for upside if maturing Phase 1 data (and readouts from newly-initiated Phase 2 trials) can support: **1)** increased duration of treatment in myeloma, DLBCL, elderly AML and sarcoma; and **2)** better defined signals of activity in additional blood cancers and/or solid tumors.

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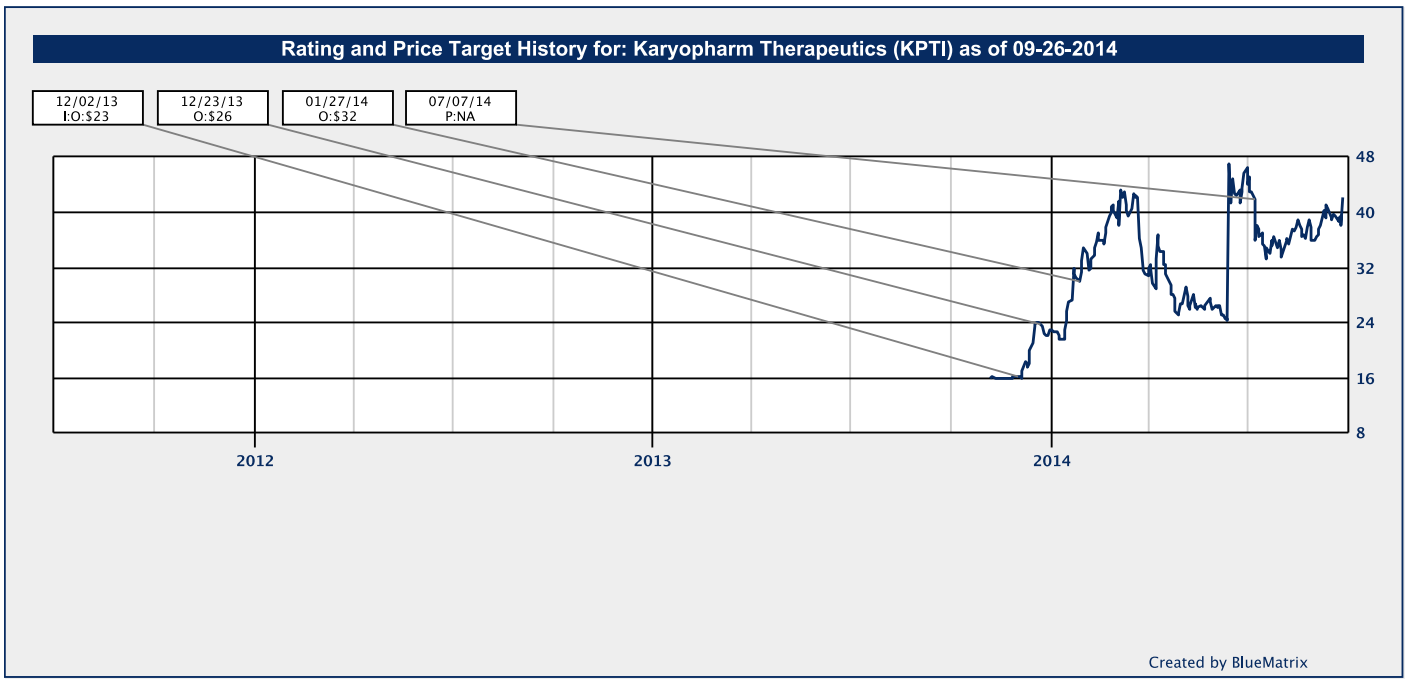

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			IB Serv/Past 12 Mos.	
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