

November 5, 2014

HEALTHCARE/BIO TECHNOLOGY

Stock Rating:

PERFORM

12-18 mo. Price Target NA
KPTI - NASDAQ \$37.71

3-5 Yr. EPS Gr. Rate NM
52-Wk Range \$47.98-\$15.50
Shares Outstanding 29.8M
Float 8.4M
Market Capitalization \$1,232.0M
Avg. Daily Trading Volume 226,588
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

Karyopharm Therapeutics

What to Look for in ASH Abstracts Tomorrow

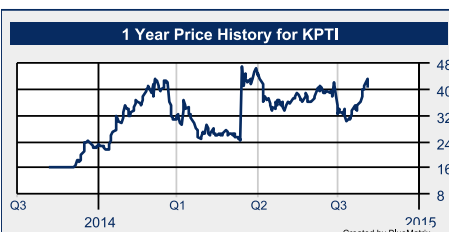
SUMMARY

ASH abstracts will be posted online at 9 AM ET tomorrow. We are expecting one KPTI abstract on the Selinexor Phase 1 in R/R myeloma. Two additional patients have been dosed at 45 mg/m² (i.e. 10 total vs. 8 at EHA) and we expect efficacy data for these remaining two patients in the abstract. Even assuming no additional responses, implied CR/PR rates of 10%/30% still compare favorably to Kyprolis' approval trial (1/266 CR (0.4%), 60/266 PR (~23%)), but investors have struggled with comparability to Kyprolis given the small Selinexor sample size. Our quick statistical analysis (see below and inside) tackles the comparability issue and suggests early data in 10 patients (EHA/ASH) may provide better insights into longer-term trends than some believe.

KEY POINTS

- **Tomorrow's myeloma abstract**, while only two more patients, expands the sample by ~25% and should incrementally clarify Selinexor's potential in myeloma. While we believe expectations are low, seeing another CR (and potentially two more PRs) would likely be enough for us to conclude that our ~5% peak share in R/R myeloma may prove too conservative.
- **Quick statistical analysis on myeloma response rates.** We can still draw some conclusions about Selinexor vs. Kyprolis, even with only 10 patients' worth of Selinexor data (see graphs inside). To illustrate, even assuming no more responses in the ASH abstract (i.e. 40% ORR) we see a >90% chance that Selinexor's true ORR exceeds Kyprolis' 23%.
- **We are not expecting any data in the abstract for 10 myeloma patients dosed at a higher 60 mg/m²,** which will have to wait for the ASH conference. However, mgmt has played down expectations for the 60 mg/m² dose, given higher than expected toxicity, and so our focus is on 45 mg/m².
- **Data Recap.** Recall at EHA Selinexor showed a 50% overall response rate (3/8 PR (37.5%), 1/8 CR (12.5%)) at 45 mg/m² + low-dose dex (~5.5 median prior lines). Kyprolis showed 1 (0.4%) CR and 60 (23%) PRs (13 VGPR, 47 PR) in 266 pts in the single-arm approval trial (5 median prior lines).
- **NHL / DLBCL.** We are also expecting an abstract on the DLBCL Phase 1 patients, with a closer look at responses by dose (3-60 mg/m²). However, the focus for the stock tomorrow is the myeloma update.

Stock Price Performance



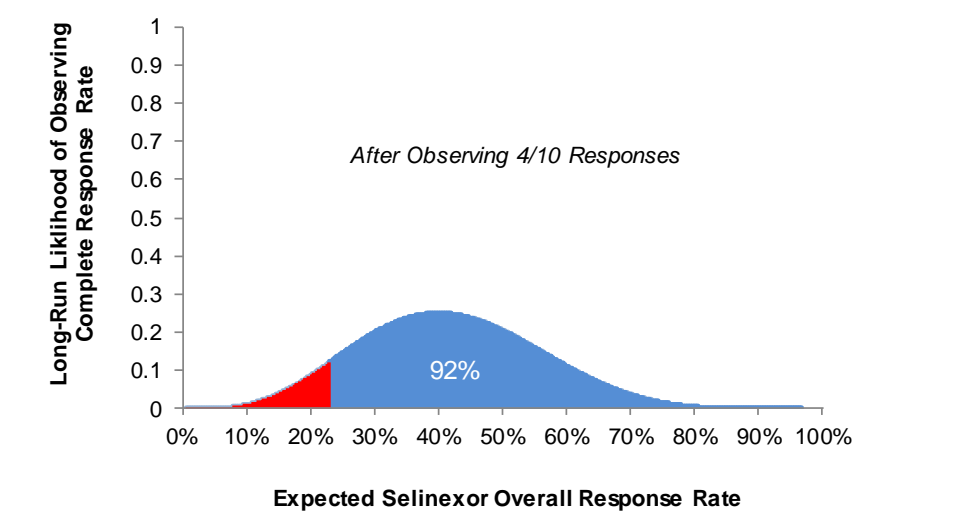
Company Description

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.

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Exhibit 1

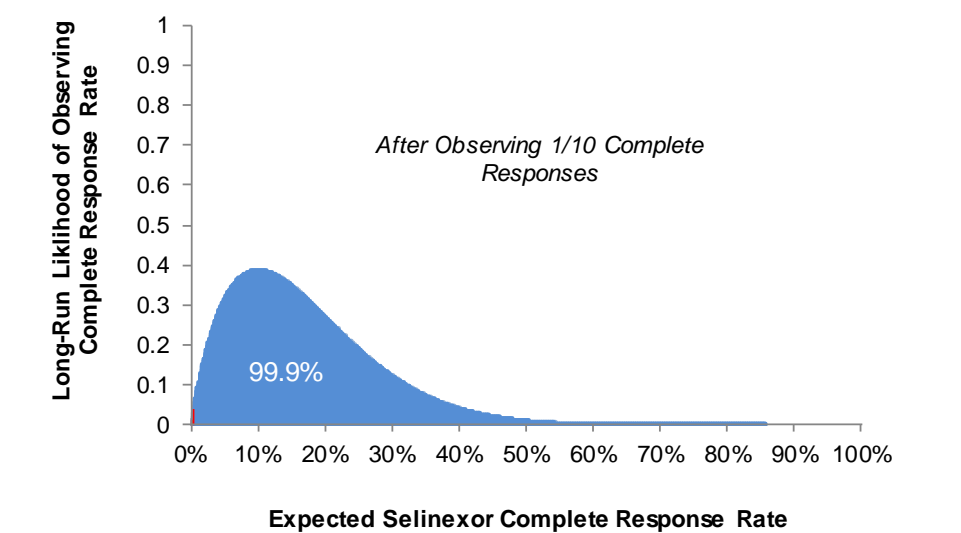
Our calculations (described below) imply 92% probability that the long-run ORR rate for Selinexor will exceed Kyprolis' 23% (61/266), even assuming the ASH abstract does not produce any more responses (i.e. 4/10).



Source: Oppenheimer Research. Red region corresponds to overall response rates favoring Kyprolis.

Exhibit 2

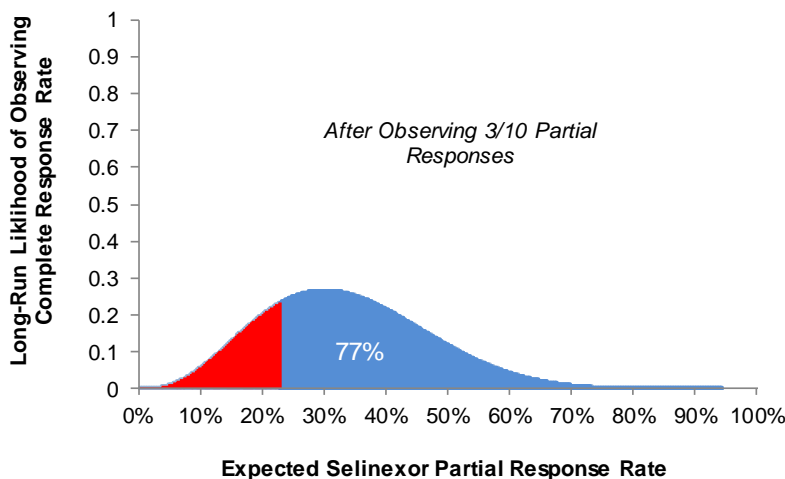
Our calculations (described below) imply 99.9% probability that the long-run CR rate for Selinexor will exceed Kyprolis' 0.4% (1/266), even assuming the ASH abstract does not produce any more CRs (i.e. 1/10).



Source: Oppenheimer Research. Tiny red region (extreme left) corresponds to complete response rates favoring Kyprolis.

Exhibit 3

Our calculations (described below) imply 77% probability that the long-run PR rate for Selinexor will exceed Kyprolis' 23% (60/266), even assuming the ASH abstract does not produce any more PRs (i.e. 3/10).



Source: Oppenheimer Research. Red region corresponds to partial response rates favoring Kyprolis.

Additional PRs or CRs in the remaining two patients in the ASH abstracts would obviously raise these odds.

Statistical Methods

We used a statistical technique called Maximum Likelihood Estimation (MLE) to gain insight into the long-run probability of CRs, PRs and ORR for Selinexor in R/R myeloma. A myeloma patient will either 1) achieve a response (we assign a probability w) or 2) will not achieve a response (we assign probability $1 - w$). If we know the probability w , and have observed y responses among n patients, the chance of observing this pattern can be determined by the binomial distribution:

$$f(y|n, w) = \frac{n!}{y!(n-y)!} w^y (1-w)^{n-y}$$

$$(0 \leq w \leq 1; y = 0, 1, \dots, n)$$

However, for the Karyopharm data we have the reverse situation. We have observed a certain data set (for instance, for PRs, $y = 3$ among $n = 10$ patients, assuming no more PRs in ASH abstract) **but we do not know the underlying probability w of a PR given the small sample size**. To gain insight into what values of w are most likely, we start with the observed data and evaluate the so-called likelihood function at all values of w (from 0 to 1):

$$L(w|n = 10, y = 3) = f(y = 3|n = 10, w)$$

$$f(y = 3|n = 10, w) = \frac{10!}{3!7!} w^3 (1-w)^7$$

$$(0 \leq w \leq 1)$$

The expression above is plotted in Exhibit 3. Further, the expression above where $y = 4$ is plotted in Exhibit 1 and where $y = 1$ in Exhibit 2.

Investment Thesis

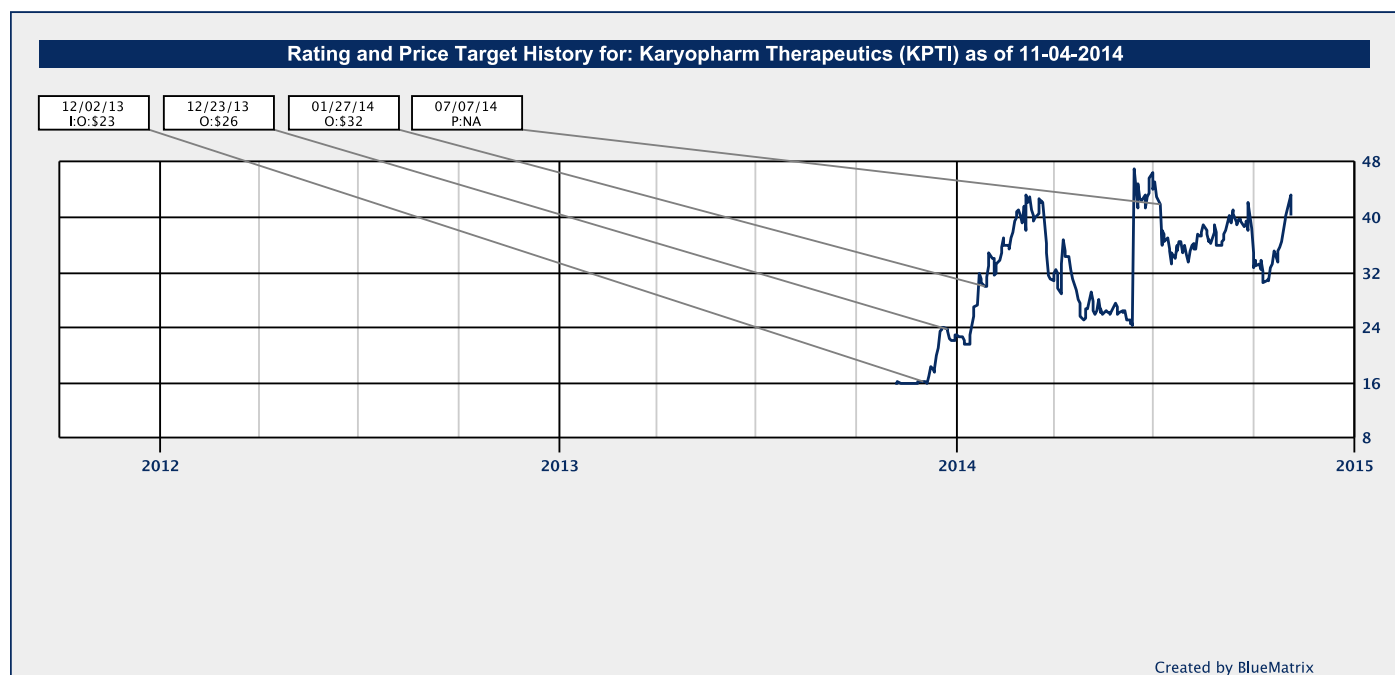
We believe Karyopharm shares are currently fairly valued. The emerging Phase 1 data for Karyopharm's lead drug Selinexor suggest to us fair-to-good chances of approval as a salvage therapy in several advanced cancers. We focus our work on myeloma, DLBCL, elderly AML and sarcoma, where we currently see 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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Distribution of Ratings/IB Services Firmwide				
Rating	Count	IB Serv/Past 12 Mos.		Count
		Percent	Percent	
OUTPERFORM [O]	321	54.68		149
PERFORM [P]	259	44.12		94
UNDERPERFORM [U]	7	1.19		0
				0.00

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