

July 7, 2014

HEALTHCARE/BIO TECHNOLOGY

Stock Rating:

**PERFORM**

12-18 mo. Price Target NA  
KPTI - NASDAQ \$42.99

3-5 Yr. EPS Gr. Rate NM  
52-Wk Range \$47.98-\$15.50  
Shares Outstanding 29.8M  
Float 8.4M  
Market Capitalization \$1,401.8M  
Avg. Daily Trading Volume 408,564  
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	(0.50)	(0.49)	(0.57)	(2.03)	NM
2015E	--	--	--	--	(3.04)	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	0.2	0.2	0.2	0.8	NM
2015E	--	--	--	--	2.0	NM

# Karyopharm Therapeutics

Good Story, But Fully Valued; Assuming Coverage with Perform

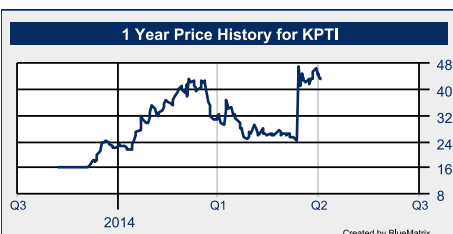
## SUMMARY

We are assuming coverage of Karyopharm with a Perform rating as we believe the shares are currently fairly valued (Oppenheimer's prior rating was Outperform). 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/duration assumptions in the R/R setting support the valuation. We see room for upside if maturing Phase 1 data (and readouts from new Phase 2 trials) can support: **1)** increased duration of treatment in myeloma/DLBCL/AML/sarcoma; and **2)** better defined signals of activity in additional blood cancers and/or solid tumors.

## KEY POINTS

- **Sarcoma.** We see potential for solid share (~30%) in advanced sarcomas given PFS of ~4 months by our analysis (Exhibit 4), which looks competitive vs. Yondelis (~2.5 months) and in line with Votrient (~4.5 months). Votrient's challenging side effect profile suggests better options may be desirable in advanced sarcoma, even if they deliver comparable efficacy.
- **AML, Myeloma & DLBCL.** We see solid efficacy across the three indications. The bar is low in R/R elderly AML, and the ~11% CR/CR(i) rate so far suggests an approvable drug. For myeloma and R/R DLBCL, the field is substantially more crowded but the data appear initially competitive, particularly in the GCB subtype for DLBCL.
- **Solid Tumors.** The Phase 1 dataset is skewed heavily toward SD as the best response (see Exhibit 13). Given the end-stage disease setting, these results may understate Selinexor's efficacy in earlier lines of therapy. Maturing Phase 1 and/or upcoming Phase 2 data (prostate, gynecologic, brain, squamous) could strengthen our view of efficacy in solid tumors.
- **Duration an upside lever.** We have estimated median PFS to drive our duration of treatment assumptions for the indications we model. Our work conservatively supports a blended median duration of therapy of ~4.5 cycles across sarcoma, AML, DLBCL and myeloma. Each additional ~1/2 month of duration could add ~\$5-6 to the valuation (Exhibit 1).

## 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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Investment Thesis

Summary & Conclusions

**We are assuming coverage of Karyopharm (KPTI) with a Perform rating as we believe the shares are currently fairly valued.** Karyopharm is a biotechnology company focused on the development of drugs that can block nuclear export of tumor suppressor proteins (via CRM1/XPO1), a novel and potentially broad-based approach to the treatment of a range of blood cancers and solid tumors. The company’s lead asset is Selinexor (KPT-330), a selective inhibitor of nuclear export (SINE), which is currently in Phase 1 testing in blood cancers, solid tumors, and sarcomas. Several Phase 2 trials are either commencing or planned including registration-directed trials in AML (acute myeloid leukemia), DLBCL (diffuse large B-cell lymphoma) and Richter’s (see our catalyst calendar, Exhibit 16).

**Our overall thesis on Karyopharm is that Selinexor has demonstrated sufficient early efficacy in the challenging salvage settings of relapsed/refractory DLBCL, multiple myeloma, elderly AML, and sarcomas** (where patients have typically exhausted remaining treatment options) **to meet our threshold for achieving proof-of-concept, despite having only generated Phase 1 dose-escalation data.** Relatively conservative share and duration assumptions in the salvage settings for these four cancers appear sufficient to support Karyopharm’s current valuation. Currently we include R/R DLBCL, MM, elderly AML and advanced sarcomas in our model and forecast peak sales of roughly ~\$1 B across these four indications. We agree with the market that, given the emerging (though early) data and the breadth of Selinexor’s mechanism in potentially finding application across multiple cancers, an approximate ~\$1B in peak Selinexor sales implied by the current valuation is a reasonable working assumption.

**We are reserving judgment on Selinexor’s potential in additional blood cancers and solid tumors, where the data continue to mature but appear to fall short of proof-of-concept in our assessment, given:** **1)** limited patient sampling (handful of patients’ worth of data), making definitive conclusions challenging; **2)** median PFS (progression-free survival) that does not appear differentiated from historical benchmarks (i.e., head and neck cancer); and/or **3)** predominance of stable disease as the best response (i.e., colorectal cancer, among others). However, as the Phase 1 data set matures and data from newly initiated Phase 2 trials (prostate, gynecologic, brain, squamous) begin to emerge, we should have opportunities to re-assess Selinexor’s potential in additional cancers.

**Share and duration are important valuation themes.** In the relapsed/refractory cancer setting, even small increments in duration (i.e. ~1 month) can add meaningfully on a percentage basis to valuation. The same holds true with peak share, where we make modest assumptions for DLBCL (~5%) and myeloma (~7%), and slightly more aggressive assumptions for AML (~21%) and sarcomas (~30%). As the data continue to mature, evidence of **1)** increased duration in patients currently on Selinexor and/or **2)** data in a greater pool of patients suggesting early conclusions on efficacy are gaining traction, could generate potential upside. As an illustration of the potential associated with greater share and duration, we flexed our model on these key variables (Exhibit 1).

Exhibit 1

Value per Share Sensitivity Analysis on Share and Duration (Base Case in Boxes)

							Peak Share							
Treatment Duration (28-day Cycles)	DLBCL					3%	4%	4%	5%	5%	5%	6%		
	Myeloma					5%	5%	6%	7%	7%	8%	8%		
			AML				14%	16%	18%	21%	23%	25%	27%	
			Sarcoma			21%	24%	27%	30%	33%	36%	39%		
					All	11%	12%	14%	15%	17%	18%	20%		
	2.1	5.4	2.5	3.0	3.2	\$12	\$16	\$19	\$23	\$27	\$31	\$35		
	2.4	6.2	2.9	3.4	3.7	\$16	\$20	\$25	\$29	\$34	\$38	\$42		
	2.7	6.9	3.2	3.8	4.2	\$20	\$25	\$30	\$35	\$40	\$45	\$50		
	3.0	7.7	3.6	4.2	4.6	\$24	\$29	\$35	\$40	\$46	\$51	\$57		
	3.3	8.5	4.0	4.6	5.1	\$28	\$34	\$40	\$46	\$52	\$58	\$64		
3.6	9.2	4.3	5.1	5.6	\$32	\$39	\$45	\$52	\$58	\$65	\$72			
3.9	10.0	4.7	5.5	6.0	\$36	\$43	\$50	\$57	\$65	\$72	\$79			

Source: Oppenheimer Research.

A ~0.5 to 1-month duration gain and a ~100-200 bps share gain (on a blended basis across the four indications we model) suggest upside potential of ~\$10-15 per share. As the data evolve, we should gain a better appreciation of where Selinexor falls on the duration/share map for relapsed/refractory DLBCL, multiple myeloma, elderly AML, and sarcomas. **Evidence of Selinexor's efficacy in additional tumors may provide another axis for potential upside, but again we need to see more data.**

**A word on Selinexor's safety profile.** We are not overly concerned here and we will not dwell on this topic, given: **1)** seemingly effective management of the principal side effect (appetite suppression) with supportive therapy (appetite stimulants); **2)** apparent easing of the AE (adverse event) burden in cycle 2+; and **3)** a clinical benefit risk/reward balance skewed to accept higher side effects provided additional efficacy can be generated in salvage cancer patients with few-to-no remaining therapeutic options. That said, our main longer-term concern on the safety profile pertains to improving the duration of therapy if curtailed by AEs. This could be an issue down the road as Selinexor is advanced into earlier lines of therapy where the balance shifts to a lower side effect burden and more durable efficacy, particularly as Selinexor is combined with other agents. For instance, taking the recent ASCO 2014 NHL data to illustrate, rates of nausea (~47%/~13% Gr.1/Gr.2), anorexia (~32%/~21% Gr.1/Gr.2), fatigue (~23%/~18%/~10% Gr.1/Gr.2/Gr.3), vomiting (~29%/~2% Gr.1/Gr.2), thrombocytopenia (~8%/~5%/~13%/~20% Gr.1/Gr.2/Gr.3/Gr.4) and neutropenia (~3%/~6%/~10%/~12% Gr.1/Gr.2/Gr.3/Gr.4) could preclude combination therapy with regimens that exhibit overlapping adverse event profiles (i.e., R-CHOP). However, combination therapy may permit lower doses of Selinexor than as a single agent, possibly mitigating this issue, so early combination data will be important to watch.

## XPO1 Development Landscape Thin

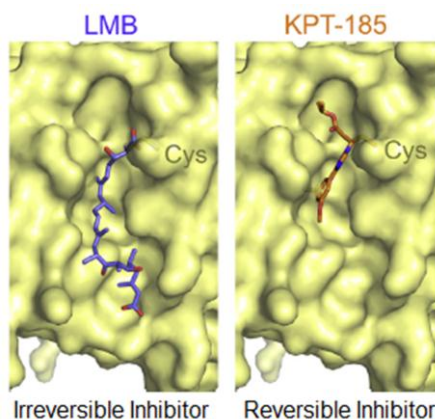
**Karyopharm appears to be the only company testing an XPO1 inhibitor in the clinic.** The potential breadth of the nuclear export target XPO1 looks attractive and it raises the natural question as to why other drug developers do not seem to be focusing on this target. We see several possible explanations:

1. Karyopharm appears to have a significant edge on the structural biology and chemical insight required to effectively develop XPO1 inhibitors (in part through heavy investment in computational drug development<sup>1</sup> for XPO1), particularly with respect to developing reversible XPO1 inhibitors.
2. The failure of the natural compound and XPO1 inhibitor leptomycin B in clinical studies may be a deterrent to investment by others. Leptomycin B was an irreversible XPO1 inhibitor that, while potent, resulted in unacceptable toxicity in pre-clinical and clinical work (largely given the irreversible binding).
3. The breadth of the nuclear export mechanism as a target, while appealing from a cancer therapy standpoint, may create valid concerns from a strategic perspective about investing in a mechanism with potentially equally broad side effects. To an extent, this concern had been borne out in Karyopharm's Phase 1 data (but so far the AEs seem to be being managed fairly well).
4. Lack of investment by big pharma and larger biotechnology companies does not imply that XPO1 is not potentially attractive. Said another way, competitors may recognize Karyopharm's expertise and development lead in the XPO1 space and would rather monitor the company's progress and make the investment (i.e. partner or even acquire the company) at a future time with more de-risked data.

**That said, there is a range of XPO1 inhibitors under investigation pre-clinically,** including ratjadone compounds, KOS-2464, FOXO export inhibitors, valtrate,

### Exhibit 2

**Karyopharm Succeeded in Developing Reversible XPO1 Inhibitors, a Key Advance over Leptomycin B (LMB)**



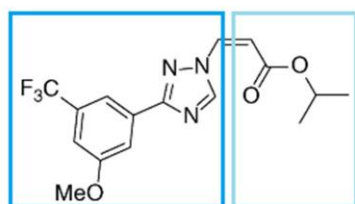
Sources: Fung, et al. "Atomic basis of CRM1-cargo recognition, release and inhibition". *Seminars in Cancer Biology* (2014) (Article in Press). Oppenheimer Research.

<sup>1</sup> Karyopharm has developed a method called Consensus Induced Fit Docking (cIFD) to computationally dock small molecule compounds into CRM1's nuclear export signal (NES) groove to identify new SINE inhibitors. See Kalid O, et al. Consensus Induced Fit Docking (cIFD): methodology, validation, and application to the discovery of novel Crm1 inhibitors. *J Comput Aided Mol Des* 2012;26:1217–28. While Karyopharm's SINEs also bind covalently to XPO1 (like leptomycin B), unlike leptomycin B the SINEs are slowly reversible, which appears to contribute to their increased tolerability.

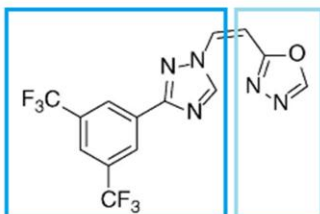
acetoxychavicol acetate, N-azolyllacrylate analogs and more recently CBS9106 (*J Cancer* 2013; 4(8):614-625; *Biochem Pharmacol.* 2012 Apr 15;83(8):1021-32). However, the apparent clinical candidates KOS-2464 (analog of the natural compound leptomycin B, developed by the former Kosan Biosciences) and CBS9106 (apparently being developed by the Japanese company CanBas) do not appear in any trials on clinicaltrials.gov. Karyopharm's position as the apparent sole clinical player for XPO1 inhibition is obviously helpful competitively, but this advantage does not lower the bar on showing differentiated efficacy vs. other mechanisms either approved or in development in relapsed/refractory cancers.

### Exhibit 3

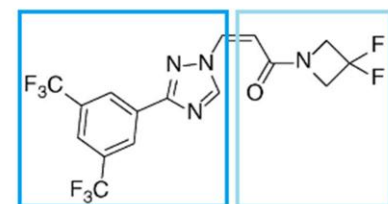
#### Karyopharm's SINEs Share a Common Chemical Design



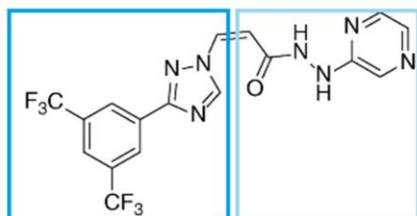
KPT-185



KPT-251



KPT-276



KPT-330

Phenyl  
triazole  
scaffoldMichael  
addition  
acceptor

Sources: <http://mct.aacrjournals.org/>. Oppenheimer Research.

### Sarcoma

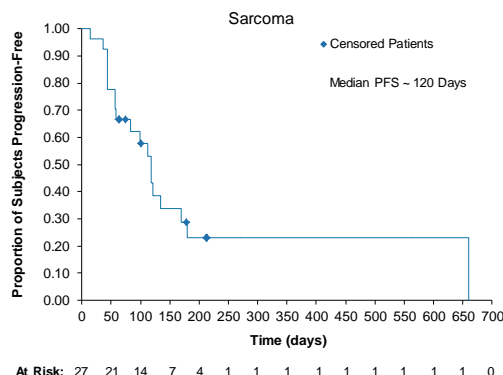
**Sarcoma data look impressive.** In the latest ASCO 2014 data, Karyopharm reported a 52% SD (stable disease) rate as the best response among 21 evaluable soft tissue and bone sarcoma patients of various subtypes (liposarcoma, leiomyosarcoma, synovial sarcoma, chondrosarcoma, osteosarcoma, among others) with 3 median prior treatments. Our understanding from physician commentary (and from examining the literature on median PFS for placebo arms of advanced sarcoma trials) is that SD in advanced sarcoma patients is clinically relevant, as this patient pool tends to progress within weeks without additional treatment. **Therefore, despite a lack of objective responses, PFS driven by stable disease appears to be a valuable gauge of clinical benefit in advanced sarcoma.**

**An initial ~4 month median PFS seems to compare favorably to historical benchmarks in advanced sarcomas for single-agent therapies.** Using duration data disclosed by Karyopharm, we generated a PFS plot and calculated a median PFS of ~120 days (see Exhibit 4, and Appendix on p. 14 for methods and assumptions). We believe this estimate is a fairly accurate approximation of current PFS in the trial, although Karyopharm has not disclosed PFS per se.

**Comp to Votrient.** Votrient achieved 4.6 months median PFS in the Phase 3 trial (PALETTE) supporting FDA approval label expansion for advanced soft tissue sarcoma, with a 4% response rate (all PRs) in arguably slightly healthier patients (56% ≥ 2 lines and 44% 0 or 1 prior line of therapy). The low overall response rate highlights that attaining SD in advanced sarcoma should be viewed as a favorable outcome. While Votrient shares toxicities seen with Selinexor (i.e., fatigue, diarrhea, nausea, decreased appetite and vomiting, among others) Votrient has also been associated with potentially life-threatening AEs (i.e., collapsed lung, heart failure, venous thrombosis, and pulmonary embolism) and carries a black box warning for hepatotoxicity. Some have argued that Votrient's safety profile is questionable in advanced soft-tissue sarcoma given the lack of an OS benefit and excessive toxicity (*Prescribe Int.* 2013 Jun;22(139):145-7). These observations suggest to us that Selinexor could play a role in advanced soft tissue sarcoma as a potentially safer option and with roughly equivalent PFS, assuming Karyopharm's current data trends are reinforced over time.

### Exhibit 4

#### Estimate of PFS for Advanced Sarcoma Patients (Oppenheimer Generated)



Sources: Karyopharm Data Presentations; Oppenheimer Research. E. L. Kaplan and Paul Meier, J. of the American Statistical Association, Vol. 53, No. 282 (Jun., 1958), pp. 457-481. See Appendix for additional details on methods and assumptions.

**Comp to Yondelis.** In Europe, the approved agent Yondelis (label for advanced soft tissue sarcoma) generated an average PFS of only ~2.5 months across five Phase 2 trials. Yondelis yielded a median PFS of 1.9 months in an uncontrolled Phase 2 study (*J Clin Oncol.* 2004 Mar 1;22(5):890-9) and a median PFS of 3.3 months in a randomized controlled trial in metastatic liposarcoma or leiomyosarcoma in patients failing anthracyclines and ifosfamide (*J Clin Oncol.* 2009;27(25):4188). In three other Phase 2 trials in advanced sarcomas, Yondelis achieved median PFS of 1.6, 1.7 and 3.5 months (*J Clin Oncol.* 2005;23(24):5484; *J Clin Oncol.* 2004;22(8):1480; *J Clin Oncol.* 2005;23(3):576). We see Selinexor's initial PFS data as somewhat more competitive than Yondelis.

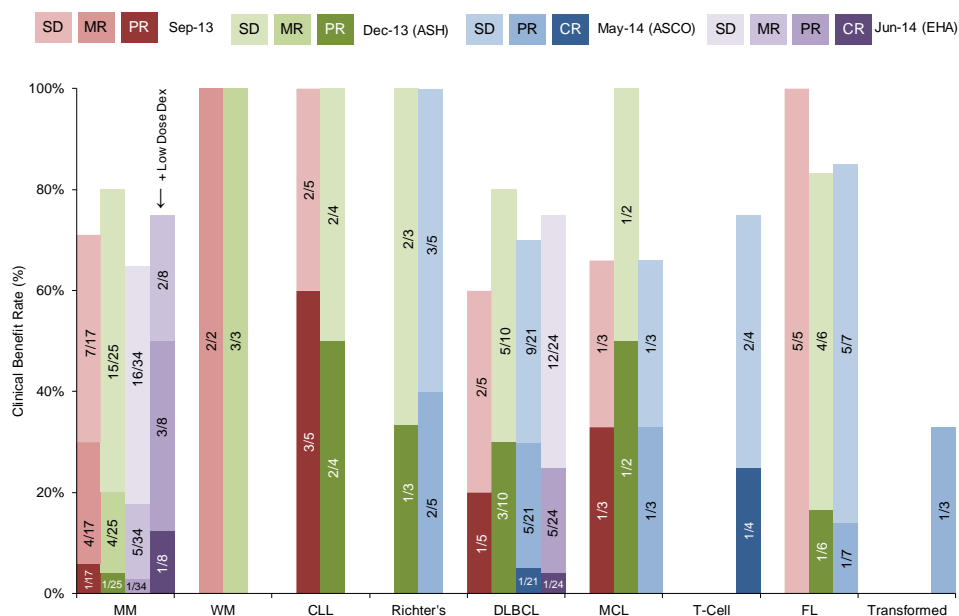
**Share & duration assumptions.** We are assuming a peak ~30% share for Selinexor in the advanced soft tissue and bone sarcoma markets (soft tissue sarcomas comprise ~80% of the incident pool), which we believe is a fair initial assumption given the PFS data and comparisons to approved agents in the US and EU. On duration, we assume the median PFS of ~4 months generated in our Kaplan-Meier analysis.

## Blood Cancers

Karyopharm is testing Selinexor in a broad range of advanced blood cancers in Phase 1 (we have summarized the data by tumor and disclosure date in Exhibit 5). We focus our work on R/R DLBCL, R/R myeloma and R/R elderly AML where we see the best opportunities for success in the data so far. Beyond these indications (i.e., for CLL, Richter's, MCL, WM, T-Cell, FL) we do not have enough data to make a call yet (Exhibit 5). However, Karyopharm is planning a Phase 2 registration directed trial in Richter's Syndrome, which bears watching.

### Exhibit 5

#### Evolution of Phase 1 Response Rates for Selinexor in Blood Cancers



Sources: Karyopharm presentations, Oppenheimer Research.

## Diffuse Large B-Cell Lymphoma (DLBCL)

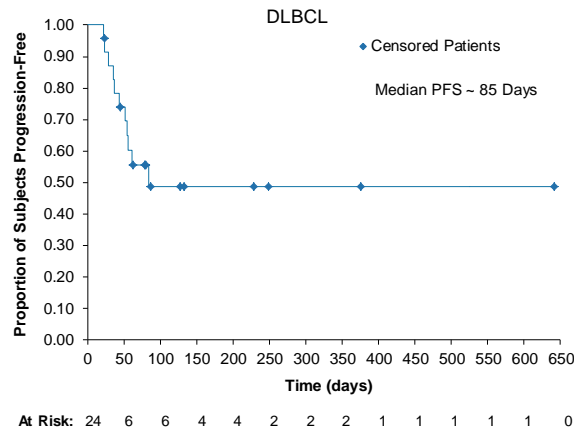
In addition to myeloma, the most comprehensive data set in blood cancers is in DLBCL (24 patients, 11 GCB, 4 non-GCB, 9 untyped). R/R DLBCL is a crowded space with many agents in development (Imbruvica, Revlimid, and Gazyva, among others). We see the Selinexor single agent data as competitive in the R/R DLBCL setting in both the GCB and non-GCB subtypes, with a 25% response rate (1 CR, 5 PR among 24 evaluable, 3.6 median prior lines of therapy) in the latest data cut at EHA (see Exhibit 5 for evolution of Phase 1 data since September 2013). **Importantly, Selinexor showed approximate equal initial efficacy in GCB (27% ORR (3/11), 1 CR, 2 PR) and non-GCB (25% ORR,**



(1/4) 1 PR) which appears to be a possible point of differentiation vs. Imbruvica and Revlimid which have largely only shown efficacy in non-GCB patients.

## Exhibit 6

### Estimate of PFS for R/R DLBCL Patients on Selinexor



Sources: Karyopharm Data Presentations; Oppenheimer Research. E. L. Kaplan and Paul Meier, J. of the American Statistical Association, Vol. 53, No. 282 (Jun., 1958), pp. 457-481. See Appendix for additional details.

**Comp to Revlimid.** Revlimid showed a similar 28% response rate (11% CR, 17% PR) in 47 R/R DLBCL patients with 4 median prior lines. The median PFS for Revlimid was 2.7 months which is directly in line with the ~85 days seen for Selinexor (see Exhibit 6). A separate retrospective study highlighted underwhelming efficacy for Revlimid in GCB patients (8.7% ORR) vs. non-GCB patients (52.9% ORR).

**Comp to Imbruvica.** Imbruvica showed a higher 41% response rate (17% CR, 24% PR) in 29 non-GCB patients, but similar to Revlimid only a 5% response rate (5% PR) in 20 GCB patients (3 median prior lines of therapy across the trial).

**Modest share assumptions in R/R DLBCL.** Selinexor appears competitive with both Revlimid and Imbruvica on efficacy, particularly in GCB patients. However, we believe hematologists may opt for Revlimid or Imbruvica first in non-GCB patients in view of Selinexor's slightly more challenging AE profile. For GCB patients, there may be a role for Selinexor ahead of Imbruvica or Revlimid in patients failing earlier lines of chemotherapy and ASCT, but we would like to see more data to solidify this conclusion. Additionally, we are cautious on Selinexor in combination with other chemotherapeutic regimens for DLBCL given potentially overlapping AE profiles. Based on these observations, we are assuming modest peak share in R/R DLBCL of ~5%. On duration (see Exhibit 6), we are assuming 3.0 cycles in line with the median PFS of ~85 days.

## Elderly Acute Myeloid Leukemia (AML)

**Elderly AML is a challenging setting where we see a relatively low bar for the adoption of new agents, particularly in the relapsed/refractory setting.** There have been several notable setbacks including Dacogen's failure to garner FDA approval for newly diagnosed AML following a missed OS endpoint vs. best supportive care. Recently, in data presented at the 2014 EHA meeting, in a Phase 3 trial (AML-001) Celgene's Vidaza failed to achieve statistical significance on OS as a maintenance regimen vs. conventional care following front-line induction chemotherapy. We understand both Dacogen and Vidaza are used off-label to an extent in R/R elderly AML, given limited effective treatment options that include retreatment with cytarabine, transfusion/growth factor support, and/or hydroxyurea. However, the failure of Dacogen and Vidaza to meet OS endpoints in earlier lines of therapy highlights likely marginal efficacy in the more recalcitrant relapsed/refractory setting.

**The evolution of the Selinexor data set in elderly AML (see Exhibit 7) suggests a very good early profile with a complete remission rate (CR) + complete remission with incomplete blood count recovery (CRi) of ~11% in a patient population where**

**the main potentially curative option is usually a stem cell transplant.** The majority of the 65 patients enrolled were heavily pre-treated (3 median prior lines of therapy) and elderly (mean age 67). Sixty-three percent of subjects were on their third or higher line of therapy and 79% had intermediate or adverse cytogenetic risk. The toxicity profile paralleled the broader Phase 1 experience with Selinexor (AEs seemed to lessen somewhat in cycle 2).

#### Exhibit 7

##### Response Rate Evolution in R/R Elderly Acute Myeloid Leukemia

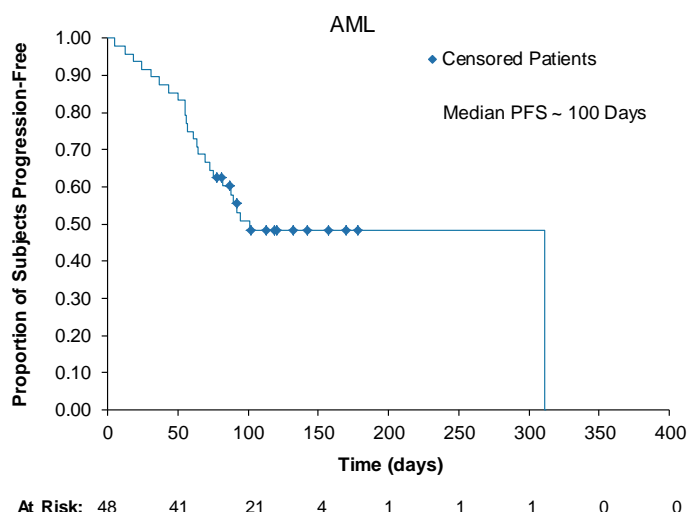
Data Cut	N	CRs+CR(i)+ PR+MF+SD	CR	CR(i)	PR	MF*	SD	PD	WC	NE
Sep-13	32	47%	6%	3%	0%	0%	38%	34%	13%	6%
Dec-13	33	52%	12%	3%	6%	3%	27%	36%	12%	-
May-14	63	49%	8%	3%	2%	3%	33%	25%	-	25%
Jun-14	65	49%	8%	3%	2%	3%	34%	25%	-	26%

Sources: Karyopharm presentations, Oppenheimer Research. \*Morphological leukemia free state.

**R/R Elderly AML response rate comps.** Given the lack of effective agents in R/R elderly AML, reasonable single-agent comps are scarce, which to an extent is why we are bullish on the ~15% overall response rate (includes morphological leukemia free state). Some broad competitors worth noting include Ambit's quizartinib, Agios' AG-221, Sunesis' vosaroxin, Boehringer Ingelheim's volasertib, and Epizyme's EPZ-5676. However, the majority of these drugs do not currently represent direct competition for Selinexor. Ambit is focused on the FLT3 mutant subtype (we assume Selinexor does not take share there, and in any case only 1 of 21 patients where FLT3 status was reported in the Selinexor trial was confirmed FLT3+), Boehringer is conducting a Phase 3 in previously *untreated* elderly AML, and Sunesis is in Phase 3 for first-relapsed or refractory (*but not elderly*) AML. While approval of quizartinib, volasertib and/or vosaroxin in earlier lines of therapy could lead to some off-label share in R/R elderly AML, we do not currently see these agents as direct competitors to Selinexor in this setting. As for Epizyme, they are focused on the MLL-r cytogenetic subtype which occurs in only ~5-10% of AML. **This leaves Agios' AG-221 (inhibitor of mutant isocitrate dehydrogenase-2, or IDH-2) as the principal competitor to Selinexor in our view.** Recent AG-221 data at the 2014 EHA meeting in 21 patients with R/R AML included 5 CR, 1 CR(i), 1CR(p) and 3 PR or a 48% overall response rate. Based on these results, Agios in collaboration with Celgene is planning to initiate in 2H14 an expansion cohort (N ~ 25) in elderly R/R AML, which we will watch closely.

#### Exhibit 8

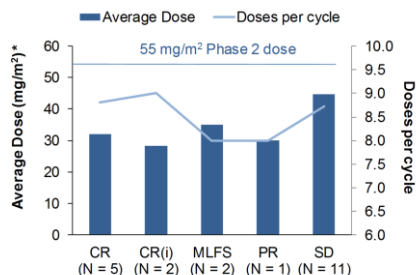
##### Estimate of PFS for Elderly AML Patients on Selinexor (Oppenheimer Generated)



Sources: Karyopharm Data Presentations; Oppenheimer Research. E. L. Kaplan and Paul Meier, J. of the American Statistical Association, Vol. 53, No. 282 (Jun., 1958), pp. 457-481. See Appendix for additional details on methods and assumptions.

## Exhibit 9

## Dose for Pivotal AML Trial Provides a Good Cushion for Efficacy Relative to Phase 1 Dose/Response Profile



Sources: Karyopharm Presentations; Oppenheimer Research. \* For patients where responses were disclosed.

**Share & duration assumptions.** We assume a peak share in R/R elderly AML of 21%. While we see the Agios IDH-2 inhibitor as a potential strong competitor, we see a 21% peak share as a reasonable base case assumption given a substantially lower bar for new therapies in R/R elderly AML vs. R/R DLBCL or R/R myeloma. On duration, we estimated a median PFS of ~100 days (see Exhibit 8) based on data provided by Karyopharm for a subset of the 65 AML patients evaluated in Phase 1 (see Appendix, p. 14, for details on our methods and assumptions). We are therefore using ~100 days (~3.6 28-day treatment cycles) as the driving assumption for treatment duration in our AML model.

**Pivotal Phase 2 underway in R/R elderly AML.** Karyopharm has commenced a pivotal randomized Phase 2 trial (SOPRA, see NCT02088541) in ~150 elderly AML patients (≥ 60 years) unfit for intensive chemotherapy or transplantation, with a primary endpoint of overall survival and a secondary endpoint of 3-month survival. The study will compare single-agent Selinexor (55 mg/m²) to physician's choice of one of three salvage therapies (best supportive care, best-supportive care + low-dose Ara-C, or best supportive care and a hypomethylating agent). The range of options permitted for the control arm reflects the challenges in designing a trial in R/R elderly AML. Recall for instance that Sunesis had generated some Phase 2 data in elderly AML (REVEAL-1 trial) which looked good (median OS 7.7 months and 1-year survival rate of 38%) but given challenges in selecting an appropriate control arm, Sunesis opted for Phase 3 in a more fit population. According to clinicaltrials.gov, we could see initial data for Selinexor's pivotal trial in April 2015. In addition to the survival endpoints, transfusion independence (while not specifically listed in clinicaltrials.gov as secondary endpoint) could provide an additional metric to assess Selinexor's potential in elderly AML. Interestingly, we do not see much of a correlation of dose with clinical outcome in the Phase 1 AML data so far (see Exhibit 9). This suggests to us that the selected dose of 55 mg/m² for the pivotal study provides a fairly good cushion to generate at least a similar efficacy spectrum as seen in the dose escalation.

## Relapsed/Refractory Multiple Myeloma

**Selinexor's early responses rate suggest some role in the salvage setting.** As a single agent, Selinexor yielded an 18% response rate (1 PR, 5 MR of 34 evaluable) and in combination with dexamethasone (dex) generated a 75% response rate (1 sCR, 3 PR, 2 MR among 8 patients) in subjects with a median of 5.7 prior lines of therapy. Although early, these results suggest some role for Selinexor in R/R myeloma. At least initially, we see the dex combination activity as more potentially competitive than Selinexor's single agent activity.

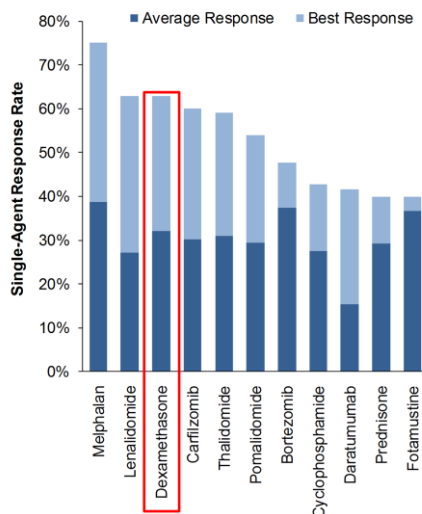
**Single agent comps.** Kyprolis as a single agent was approved on a 22.9% response rate (0.4% CR, 4.9% VGPR, 17.7% PR) in 266 patients with a median of 5 prior lines of therapy, which appears stronger than Selinexor's initial data given the higher representation of PRs. On the other hand, Pomalyst's single agent activity in heavily pre-treated myeloma was unremarkable (7.4% response rate (8/108), 8 PR) based on the Phase 2 trial supporting accelerated approval. Revlimid provides the toughest comp and as a single agent showed a 44% response rate (5 CR, 53 PR, 40 MR) in 222 R/R patients (67% ≥ 3 prior lines) (*Blood*. 2009 Jul 23;114(4)). **Therefore, while the data are still evolving, our initial impression is that Selinexor + dexamethasone will be required to be competitive in R/R myeloma.**

**However, it is worth pointing out that Selinexor's 18% response rate is among the better responses seen across a wide range of single agents tested in myeloma.** In a very recent review (see Kortuem, KM et al. *Clinical Lymphoma, Myeloma & Leukemia*, December 28, 2013 epub; article in press) of 129 drugs tested as single agents in Phase 1/2 myeloma trials, the mean response rate was ~6% (8% when considering the best response) and ~73% of the drugs did not achieve a response rate over 10%. When excluding inactive drugs, the median response was only still ~10% (~13.5% when considering the best response) among 54 active drugs.

**Myeloma Selinexor Dexamethasone Combo Data at EHA.** Investors reacted enthusiastically to data presented at the recent EHA meeting showing a 50% overall response rate and a 75% clinical benefit rate for Selinexor + low-dose dexamethasone (dex) in 8 relapsed/refractory multiple myeloma patients. These data compare favorably to results for approved myeloma drugs (Pomalyst, Revlimid and Kyprolis) also tested in combination with low-dose dex in similarly pre-treated R/R multiple myeloma patients (Exhibit 11). We agree with the market that the early Selinexor + dex combination data

## Exhibit 10

## Dexamethasone is Among the Most Potent Single-Agent Therapies in Multiple Myeloma



Source: "Activity of 129 Single-Agent Drugs in 228 Phase I and II Clinical Trials in Multiple Myeloma". Kortuem, KM et al. *Clinical Lymphoma, Myeloma & Leukemia*, 2014 (Article in Press). Figure 6 of article reproduced for clarity by Oppenheimer Research.



appear to have established a good early footing relative to Celgene's immunomodulator franchise and the proteasome inhibitor Kyprolis. Nevertheless, **1)** the small (N = 8) sample size is prone to high variability so we need more data to confirm these initial findings, and **2)** dex alone is one of the most potent single agents for multiple myeloma therapy (see Exhibit 10), so the results appear less unexpected to us than the market's initial reaction to the data would imply.

**Thoughts on combo AE profile.** Toxicity did not appear additive relative to Selinexor monotherapy, which is important. In fact, although the sample size for safety is small (N = 6), there was only 1 case of Grade 1 nausea and 1 case of Grade 2 dehydration across the entire AE table for the combo. While shorter duration of therapy is likely playing a role in generating less AEs vs. the longer-running monotherapy arms, **we also wonder whether co-medication with dexamethasone could be easing the AE burden for Selinexor. We will watch the emerging data closely to monitor this potential trend.**

#### Exhibit 11

##### Similar Response Rates in R/R Multiple Myeloma for Key Myeloma Drugs + Low Dose Dex vs. Selinexor + Low Dose Dex

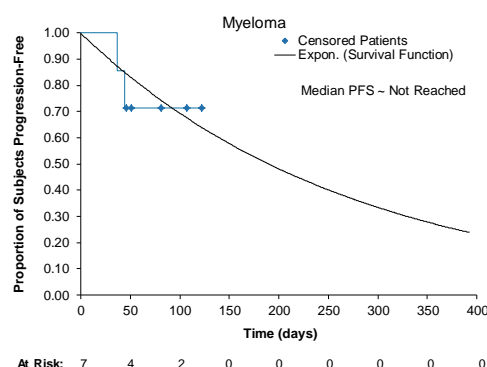
	Pomalyst + Low Dose Dex	Revlimid + Low Dose Dex	Kyprolis + Low Dose Dex	Selinexor + Low Dose Dex
<b>Patients (N)</b>	<b>113</b>	<b>187</b>	<b>20</b>	<b>8</b>
Median PFS	4.2	8.3	NA	NA
<b>ORR (≥ PR)</b>	<b>33%</b>	<b>48%</b>	<b>55%</b>	<b>50%</b>
<b>≥ MR</b>	<b>45%</b>	<b>48%</b>	<b>55%</b>	<b>75%</b>
CR	3%	4%	0%	13%
PR	30%	44%	55%	38%
MR	12%	0%	0%	25%
SD	37%	47%	30%	0%
<b>Median prior therapies (range)</b>	<b>5 (2-13)</b>	<b>4 (1-15)</b>	<b>4 (1-9)</b>	<b>5.5 (3-7)</b>
<b>Dex Dose</b>	40 mg/week	Age ≤75 40 mg/week, age >75 20 mg/week	20 mg/week (40 mg during rest week)	20 mg

Sources: 2014 EHA Abstract P953, Blood. Mar 20, 2014; 123(12): 1826–1832, Hou et al. Journal of Hematology & Oncology 2013, 6:41, ASH 2012 Abstract 4036, Oppenheimer Research.

**Modest share assumptions.** Overall, we see some role for Selinexor in R/R myeloma given the early positive trends in combination with dexamethasone. However, given the small sample size supporting the high response rates reported at EHA 2014, we are assuming a conservative ~7% peak share in R/R myeloma.

#### Exhibit 12

##### Estimates of PFS for R/R Myeloma Patients on Selinexor (Oppenheimer Generated)



Sources: Karyopharm Data Presentations; Oppenheimer Research. E. L. Kaplan and Paul Meier, J. of the American Statistical Association, Vol. 53, No. 282 (Jun., 1958), pp. 457-481. See Appendix for additional details on methods and assumptions.

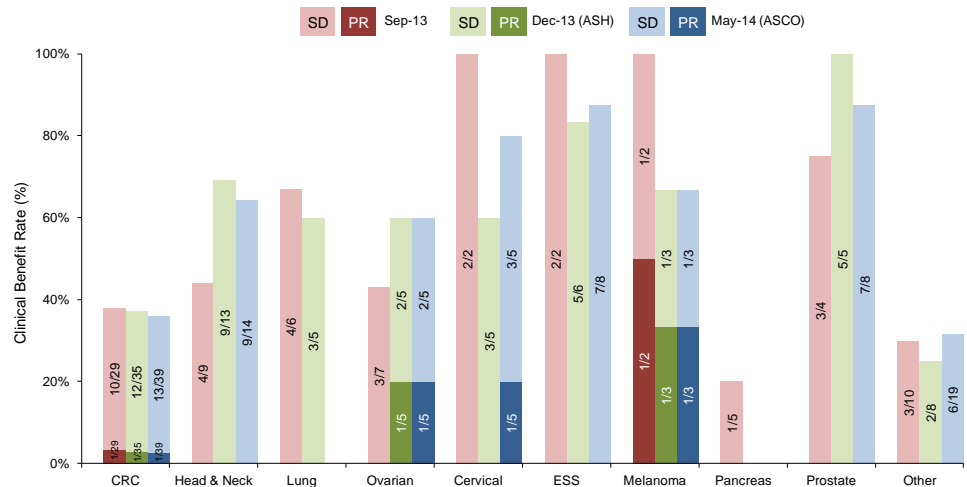
**Duration assumptions.** We generated a PFS curve for the dex combination patients (see Exhibit 12) and the median has not been reached. An exponential fit to the limited data (see Exhibit 12, black trend line), albeit crude, suggests a median PFS of ~200 days. To provide some basis to support our ~200-day assumption, we examined PFS data from several combination studies of Pomalyst + dex (i.e., IFM 2009-02 Phase 2, 6.3 months; MM-003 3.7 months; separate Phase 2 11.6 months, see *J Clin Oncol*. 2009 Oct. 20;27(30)) which collectively suggest a mean PFS of 7.2 months, consistent with our base case model assumption of ~7 months (or ~7.7 28-day cycles).

## Solid Tumors

**Too early to draw conclusions.** In our assessment, the majority of the solid tumor data falls into two categories: **1)** tumors with mainly stable disease with what we consider a critical mass of data (i.e., colorectal with 39 evaluable and only 1 PR, and head and neck, with 15 evaluable and 9 SD), or **2)** tumors with insufficient data (less than ~10 patients worth) to draw any conclusions (Exhibit 13). Therefore, we are reserving judgment on the solid tumor front for now.

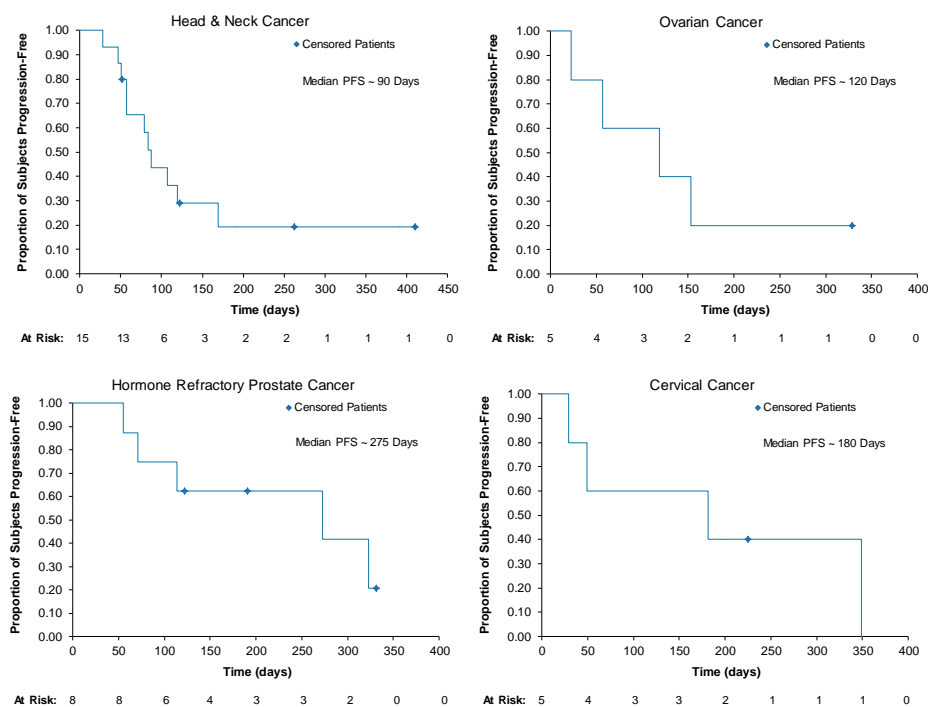
### Exhibit 13

#### Evolution of Phase 1 Response Rates for Selinexor in Advanced Solid Tumors



Source: Karyopharm presentations, Oppenheimer Research. ESS = Endometrial Stromal Sarcoma.

**PFS Estimates.** We generated PFS plots for tumors where Karyopharm provided duration data with responses (see Exhibit 14). There are some intriguing early signals, such as an apparent initial median PFS of ~275 days in hormone refractory prostate cancer; however, there are only a handful of patients on whom to base this conclusion. In head & neck, while the sampling is somewhat better, our calculated median PFS of ~90 days, at least initially, does not appear overwhelming relative to afatinib (16 weeks, see *J Clin Oncol* 2010;28 15 Suppl. Abstr 5501) or chemotherapy (3.3 months for platinum + 5-FU in the control arm of the Erbitux approval trial for recurrent/metastatic head & neck cancer). On cervical and ovarian, the PFS data are too noisy to interpret at this point. We have not seen time on study data for colorectal, so we could not estimate PFS; however, based on the response data we suspect the PFS was light. In addition to the evolving Phase 1 data set, results from newly initiated Phase 2 trials (prostate, gynecologic, brain, squamous) should provide new opportunities to examine Selinexor's potential in additional solid tumors.

**Exhibit 14****Estimates of PFS for Solid Tumor Patients on Selinexor (Oppenheimer Generated)**

Sources: Karyopharm Data Presentations; Oppenheimer Research. E. L. Kaplan and Paul Meier, J. of the American Statistical Association, Vol. 53, No. 282 (Jun., 1958), pp. 457-481. See Appendix for additional details on methods and assumptions.

## Quick Background on XPO1

Exportin1 (XPO1) is the best characterized of seven nuclear export proteins discovered. XPO1 is responsible for export of >200 proteins from the nucleus to the cytoplasm, including the majority of tumor suppressor proteins. Cancer cells up-regulate XPO1 and increase the export of tumor suppressor proteins from the nucleus, promoting resistance by shutting down cellular machinery for programmed cell death (apoptosis) in genetically aberrant cells. Karyopharm's therapeutic strategy is to inhibit XPO1 with SINE compounds such as Selinexor, driving accumulation of tumor suppressor proteins in the nucleus and thereby re-engaging the programmed cell death pathway in cancerous cells. The breadth of the XPO1-based mechanism suggests potential in a wide range of malignancies (and potentially inflammatory and viral disorders as well). On the other hand, because proper nuclear export is critical for normal cells, there is potential for broad toxicity, as was seen with leptomycin B, an irreversible XPO1 inhibitor. Karyopharm has developed SINEs that reversibly bind XPO1, opening the door for therapeutic intervention using this target.

## Valuation

Our DCF valuation suggests a value for Karyopharm in the low \$40s (where the stock currently trades) supporting our Perform rating on the company.

### Exhibit 15

#### DCF Valuation

Time of Valuation	Jun-14
<b>WACC</b>	<b>15.0%</b>
Intermediate CF Growth (2025 - 2033)	15%
Terminal FCF Growth	0.0%
Discounted FCF (2014-2033) \$MM	\$986.9
Terminal FCF Value \$MM	\$102.2
Total PV FCF \$MM	\$1,089.1
Cash \$MM 2Q14	\$229.9
Debt \$MM	\$0.0
<b>Equity Value \$MM</b>	<b>\$1,319.0</b>
Shares Outstanding (MM) 2Q14	32.6

<b>DCF Value / Share</b>	<b>\$40.46</b>
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Source: Oppenheimer Research Estimates.

**Valuation Method:** We value Karyopharm using a discounted cash flow (DCF) analysis with a WACC of 15% and a 0% terminal growth rate post 2033. Since we model the cash cost of options, we use the basic share count to avoid double-counting.

**Discount Rate:** Our valuation framework utilizes a 15% discount rate for pre-commercial stage companies given a higher risk profile than commercial stage (where we use 10%).

**Terminal Growth Rate:** We explicitly model cash flows to 2024. From 2025-2032, we grow cash flows at 15% of the prior year's rate. Given the pending Selinexor patent in 2032 and no credit for Hatch-Waxman extensions (with a projected 2017 launch, exclusivity is capped at 14 years), we decline cash flows by 50% in 2033. After 2033, we assume a terminal growth rate of 0% given the availability of a generic Selinexor, yielding a terminal value of \$102 million.

### Exhibit 16

#### Catalyst Calendar

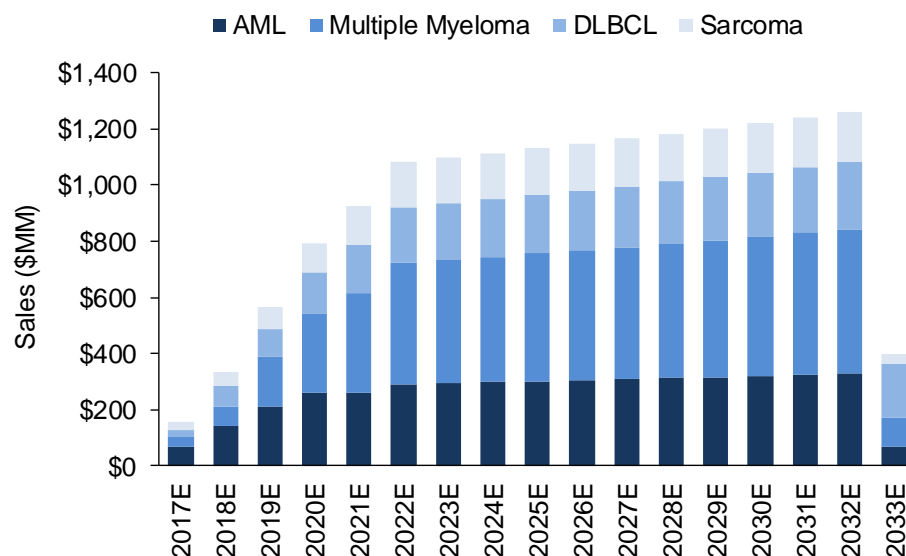
Drug	Type	Event	Timing
Selinexor	Clinical Data	Potential for Phase 1 Updates at ESMO/ASH	2H14
Selinexor	Clinical Data	Pivotal R/R Richter's Transformation (SIRRT) Phase 2 Readout	4Q14
Selinexor	Clinical Data	Metastatic Hormone Refractory Prostate Phase 2 Readout	4Q14
Selinexor	Clinical Data	Pivotal Trial (SOPRA) in R/R Elderly AML Phase 2 Readout	1H15
Selinexor	Clinical Data	Advanced Ovarian and Cervical Cancers Phase 2 Readout	Mid-2015
Selinexor	Clinical Data	Recurrent Glioblastoma after Failure of Radiation and Temozolomide (KING) Phase 2 Readout	Mid-2015
Selinexor	Clinical Data	Pivotal R/R DLBCL Phase 2 Readout	2015
Selinexor	Clinical Data	Pre-Treated Head and Neck Squamous Cell Phase 2 Readout	2015

Source: Karyopharm Filings.

## Market Model Sales Projections

### Exhibit 17

#### Worldwide Sales Projections for Modeled Indications from Launch to Patent Expiry



Source: Oppenheimer Research Estimates.

## Investment Risks

Key risks include: **1)** Selinexor's efficacy in modeled indications (DLBCL, elderly AML, myeloma, and sarcomas) may fail to gain validation with additional clinical data. **2)** Although there are currently no clinical competitors, a pre-clinical XPO1/CRM1 inhibitor with better safety or efficacy characteristics than Selinexor could be advanced into the clinic. **3)** Costs to develop Selinexor across a potentially broad range of blood cancers and solid tumors may exceed our projections, leading to a financing gap. **4)** Karyopharm will likely require additional dilutive capital before reaching commercial stage. **5)** Karyopharm may be unsuccessful in commercializing Selinexor independently (as we currently model) in the US and EU. **6)** Current issued US patents (specifically US patent No. 8,513,230) cover composition of matter for related SINEs but not for Selinexor. The filed composition of matter patent specific to Selinexor (with expected protection through 2032) is still under review by the USPTO.



## Appendix: Methods & Assumptions on Kaplan Meier PFS Plots

We developed a Kaplan Meier algorithm + graphing program (Excel-based) to generate the PFS plots in Exhibits 4, 6, 8, 12, and 14, based on the original methods outlined in E. L. Kaplan and Paul Meier's original paper (see J. of the American Statistical Association, Vol. 53, No. 282 (Jun., 1958), pp. 457-481). We used the duration data (either numerical, in the case of AML and myeloma; or bar charts, in the case of solid tumors and sarcoma) disclosed in Karyopharm's 2014 ASCO and 2014 EHA presentations. Bar chart durations were measured to the nearest day by reproduction in Excel with overlay to the original data.

**Solid Tumors.** Our general understanding from management commentary is that the majority of stable disease patients came off for progressive disease. Since we do not have access to the underlying patient records, a minority of patients may have come off the study for an AE or withdrew consent, and thus would not be classified as a progression. **Therefore, we may be modestly understating the PFS curve and median PFS in our analysis. However, we do not believe that our overall conclusions would change meaningfully.**

**AML.** Several assumptions were made in generating the AML PFS curve, given partial information: **1)** we do not have data on the timing of progression for the 16 PDs. We therefore assumed that the 16 PDs were distributed evenly from the start of the trial and ending at the mean duration of the SDs, or 102 days. **2)** We did not have duration data for 11 additional SDs. We assumed that these 11 patients would likely behave similarly to the 11 SDs where duration data was provided, i.e. a mean time on study of 102 days. **3)** CRs (5), CR(i)s (2), MLFS (2), PR (1), and SDs still on study (2) were censored<sup>2</sup>. **4)** The 9 SDs no longer on study (highlighted in Karyopharm's presentations) were assumed to have progressed. **5)** We assumed that the 11 additional SDs not highlighted at a patient level by Karyopharm remained on study and were censored. **6)** We did not include the 17 non-evaluable patients in our analysis.

**Myeloma.** We excluded the one non-evaluable patient and considered the 1 PR at day 45 who came off study to have progressed. The other five patients remaining on study were censored.

**DLBCL.** Karyopharm disclosed the PFS curve. To provide consistent formatting in our exhibits, we used our algorithm to regenerate the curve. Our work is superimposable with Karyopharm's DLBCL curve.

**PFS vs. TTP.** Finally, we chose to estimate progression free survival (PFS) and not time to progression (TTP) because using TTP would require assuming that no one came off study due to a death (TTP does not include deaths whereas PFS does). Although we understand that most patients came off study due to progressive disease (PD) not death, we do not know this with certainty.

<sup>2</sup> Censoring a patient in a Kaplan Meier analysis has nothing to do with the traditional meaning of the word censor, which can often lead to significant confusion. Censoring is a statistical method to handle patient data when you know they did not progress (in the case of PFS) or did not die (in the case of OS) through time X, but beyond that, no information on their status is available, so they are excluded from the at-risk pool of patients.

**Exhibit 18****Karyopharm Income Statement**

\$MMs except per share data

	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Selinexor Sales	0.0	0.0	0.0	0.0	0.0	155.0	336.5	566.1	795.0	923.7	1,083.7	1,099.3	1,115.3
Contract & Grant Revenue	0.6	0.4	0.8	2.0	3.0	4.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
<b>Total Revenue</b>	<b>0.6</b>	<b>0.4</b>	<b>0.8</b>	<b>2.0</b>	<b>3.0</b>	<b>159.0</b>	<b>341.5</b>	<b>571.1</b>	<b>800.0</b>	<b>928.7</b>	<b>1,088.7</b>	<b>1,104.3</b>	<b>1,120.3</b>
COGS	0.0	0.0	0.0	0.0	0.0	31.0	50.5	56.6	79.5	83.1	97.5	98.9	89.2
R&D	14.1	28.5	50.9	89.0	133.6	167.0	102.4	142.8	160.0	139.3	130.6	88.3	78.4
SG&A	2.4	5.9	13.2	18.4	48.0	96.4	139.6	143.2	146.4	149.8	152.9	154.3	155.9
<b>Operating Income</b>	<b>(15.9)</b>	<b>(34.0)</b>	<b>(63.3)</b>	<b>(105.5)</b>	<b>(178.6)</b>	<b>(135.3)</b>	<b>48.9</b>	<b>228.5</b>	<b>414.1</b>	<b>556.5</b>	<b>707.7</b>	<b>762.7</b>	<b>796.7</b>
Interest Income	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.2	0.3	0.4	0.6	0.8	1.0
Interest Expense	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
<b>Pre-Tax Income</b>	<b>(15.9)</b>	<b>(33.9)</b>	<b>(63.2)</b>	<b>(105.4)</b>	<b>(178.5)</b>	<b>(135.2)</b>	<b>49.1</b>	<b>228.7</b>	<b>414.4</b>	<b>556.9</b>	<b>708.3</b>	<b>763.4</b>	<b>797.8</b>
Tax Expense (Benefit)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	66.3	194.9	247.9	267.2	279.2
Tax Rate	NM	NM	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	16.0%	35.0%	35.0%	35.0%	35.0%
<b>Net Income (GAAP)</b>	<b>(15.9)</b>	<b>(33.9)</b>	<b>(63.2)</b>	<b>(105.4)</b>	<b>(178.5)</b>	<b>(135.2)</b>	<b>49.1</b>	<b>228.7</b>	<b>348.2</b>	<b>362.0</b>	<b>460.4</b>	<b>496.2</b>	<b>518.5</b>
<b>GAAP EPS</b>	<b>(\$8.95)</b>	<b>(\$5.59)</b>	<b>(\$2.03)</b>	<b>(\$3.04)</b>	<b>(\$4.57)</b>	<b>(\$3.11)</b>	<b>\$1.06</b>	<b>\$4.93</b>	<b>\$7.47</b>	<b>\$7.74</b>	<b>\$9.81</b>	<b>\$10.54</b>	<b>\$11.00</b>
Avg. Shares Out. - Basic	1.8	6.1	31.2	34.6	39.1	43.5	45.8	46.1	46.4	46.6	46.8	47.0	47.1
Avg. Shares Out. - Diluted	1.8	6.1	31.2	35.1	39.5	43.8	46.1	46.4	46.6	46.8	46.9	47.1	47.1

Sources: Oppenheimer &amp; Co. Inc. Estimates, Karyopharm Filings.

**Exhibit 19****Karyopharm Balance Sheet**

\$MMs except per share data

	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
<b>Assets</b>													
Cash and Equivalents	0.4	156.0	212.5	256.2	254.5	328.6	392.6	641.3	1,011.1	1,391.2	1,871.4	2,383.1	2,917.3
Prepaid Expenses and Other Current Asset:	0.6	2.0	0.8	4.3	7.3	11.8	11.7	13.7	15.4	14.9	15.2	13.7	12.9
<b>Current Assets</b>	<b>1.0</b>	<b>158.0</b>	<b>213.2</b>	<b>260.5</b>	<b>261.8</b>	<b>340.4</b>	<b>404.3</b>	<b>655.0</b>	<b>1,026.6</b>	<b>1,406.1</b>	<b>1,886.6</b>	<b>2,396.7</b>	<b>2,930.2</b>
Property, Plant, & Equipment	0.3	0.2	0.9	2.2	3.7	5.2	5.1	5.1	5.2	5.4	5.5	5.5	5.4
Deposits	0.3	-	-	-	-	-	-	-	-	-	-	-	-
Other	0.0	0.0	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
<b>Total Assets</b>	<b>1.6</b>	<b>158.2</b>	<b>215.5</b>	<b>264.1</b>	<b>266.9</b>	<b>346.9</b>	<b>410.8</b>	<b>661.4</b>	<b>1,033.2</b>	<b>1,412.9</b>	<b>1,893.5</b>	<b>2,403.6</b>	<b>2,937.0</b>
<b>Liabilities</b>													
Accounts Payables	1.1	1.7	2.8	5.4	9.1	14.7	14.6	17.1	19.3	18.6	19.1	17.1	16.2
Accrued Liabilities	0.8	1.2	2.1	4.3	7.3	11.8	11.7	13.7	15.4	14.9	15.2	13.7	12.9
Deferred Revenue	0.1	0.1	-	-	-	-	-	-	-	-	-	-	-
Other	0.0	0.3	-	-	-	-	-	-	-	-	-	-	-
<b>Current Liabilities</b>	<b>1.9</b>	<b>3.3</b>	<b>4.9</b>	<b>9.7</b>	<b>16.3</b>	<b>26.5</b>	<b>26.3</b>	<b>30.8</b>	<b>34.7</b>	<b>33.5</b>	<b>34.3</b>	<b>30.7</b>	<b>29.1</b>
Preferred Stock Subscription	9.0	-	-	-	-	-	-	-	-	-	-	-	-
Series A Convertible Preferred	18.3	-	-	-	-	-	-	-	-	-	-	-	-
Series B Convertible Stock	-	-	-	-	-	-	-	-	-	-	-	-	-
Other Liabilities	-	-	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
<b>Total Liabilities</b>	<b>29.2</b>	<b>3.3</b>	<b>5.1</b>	<b>9.8</b>	<b>16.5</b>	<b>26.7</b>	<b>26.5</b>	<b>31.0</b>	<b>34.9</b>	<b>33.7</b>	<b>34.5</b>	<b>30.9</b>	<b>29.3</b>
<b>Shareholders' Equity</b>	<b>(27.6)</b>	<b>154.9</b>	<b>210.4</b>	<b>254.3</b>	<b>250.4</b>	<b>320.3</b>	<b>384.3</b>	<b>630.4</b>	<b>998.3</b>	<b>1,379.2</b>	<b>1,859.0</b>	<b>2,372.7</b>	<b>2,907.7</b>
<b>Total Liabilities &amp; Equity</b>	<b>1.6</b>	<b>158.2</b>	<b>215.5</b>	<b>264.1</b>	<b>266.9</b>	<b>346.9</b>	<b>410.8</b>	<b>661.4</b>	<b>1,033.2</b>	<b>1,412.9</b>	<b>1,893.5</b>	<b>2,403.6</b>	<b>2,937.0</b>

Sources: Oppenheimer &amp; Co. Inc. Estimates, Karyopharm Filings.

**Exhibit 20****Karyopharm Cash Flow Statement**

\$MMs except per share data

	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Net Income	(15.9)	(33.9)	(63.2)	(105.4)	(178.5)	(135.2)	49.1	228.7	348.2	362.0	460.4	496.2	518.5
Depreciation & Amortization	0.1	0.1	0.3	0.8	1.7	2.7	3.2	3.6	3.7	3.6	3.8	3.8	3.8
Share-Based Compensation	0.7	3.8	4.9	5.4	9.1	14.7	14.6	17.1	19.3	18.6	19.1	17.1	16.2
Other	-	0.1	-	-	-	-	-	-	-	-	-	-	-
<b>Total Operating Sources</b>	<b>(15.1)</b>	<b>(29.9)</b>	<b>(58.1)</b>	<b>(99.2)</b>	<b>(167.8)</b>	<b>(117.8)</b>	<b>66.9</b>	<b>249.4</b>	<b>371.2</b>	<b>384.2</b>	<b>483.2</b>	<b>517.1</b>	<b>538.5</b>
Prepaid Expenses and other current assets	(0.2)	(1.4)	1.2	(3.5)	(3.0)	(4.5)	0.1	(2.0)	(1.7)	0.5	(0.4)	1.6	0.7
Deposits	-	-	-	-	-	-	-	-	-	-	-	-	-
Accounts Payable	(0.1)	0.7	1.1	2.6	3.7	5.6	(0.1)	2.5	2.2	(0.7)	0.4	(2.0)	(0.9)
Accrued Expenses and other	0.0	0.4	0.9	2.2	3.0	4.5	(0.1)	2.0	1.7	(0.5)	0.4	(1.6)	(0.7)
Deferred Revenue	(0.1)	0.0	(0.1)	-	-	-	-	-	-	-	-	-	-
Other	-	-	(1.0)	-	-	-	-	-	-	-	-	-	-
<b>Changes in Operating Assets/Liabilities</b>	<b>(0.4)</b>	<b>(0.4)</b>	<b>2.2</b>	<b>1.2</b>	<b>3.7</b>	<b>5.6</b>	<b>(0.1)</b>	<b>2.5</b>	<b>2.2</b>	<b>(0.7)</b>	<b>0.4</b>	<b>(2.0)</b>	<b>(0.9)</b>
<b>Operating Cash Flow</b>	<b>(15.5)</b>	<b>(30.3)</b>	<b>(55.9)</b>	<b>(98.0)</b>	<b>(164.0)</b>	<b>(112.1)</b>	<b>66.8</b>	<b>251.9</b>	<b>373.4</b>	<b>383.5</b>	<b>483.7</b>	<b>515.2</b>	<b>537.6</b>
Capital Expenditures	(0.1)	(0.1)	(0.9)	(2.0)	(3.0)	(3.9)	(2.9)	(3.2)	(3.5)	(3.4)	(3.5)	(3.5)	(3.4)
Proceeds/Purchase of Securities	-	-	-	-	-	-	-	-	-	-	-	-	-
Other	-	-	(0.4)	-	-	-	-	-	-	-	-	-	-
<b>Investing Cash Flow</b>	<b>(0.1)</b>	<b>(0.1)</b>	<b>(1.3)</b>	<b>(2.0)</b>	<b>(3.0)</b>	<b>(3.9)</b>	<b>(2.9)</b>	<b>(3.2)</b>	<b>(3.5)</b>	<b>(3.4)</b>	<b>(3.5)</b>	<b>(3.5)</b>	<b>(3.4)</b>
Issuance/Purchase of Stock	0.0	113.2	113.6	143.8	165.3	190.1	-	-	-	-	-	-	-
Issuance/Payment Convertible Notes	-	-	-	-	-	-	-	-	-	-	-	-	-
Proceeds/Purchase of Preferred Stock	2.0	-	-	-	-	-	-	-	-	-	-	-	-
Proceeds/Purchase of Convertible Preferred	7.5	72.4	-	-	-	-	-	-	-	-	-	-	-
Other	-	0.3	-	-	-	-	-	-	-	-	-	-	-
<b>Financing Cash Flow</b>	<b>9.5</b>	<b>185.9</b>	<b>113.6</b>	<b>143.8</b>	<b>165.3</b>	<b>190.1</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>
Effect of Exchange Rates	-	-	-	-	-	-	-	-	-	-	-	-	-
Beginning Cash	6.5	0.4	156.0	212.4	256.2	254.5	328.6	392.6	641.3	1,011.1	1,391.2	1,871.4	2,383.1
Net Increase (Decrease) in Cash	(6.1)	155.6	56.5	43.8	(1.7)	74.1	64.0	248.7	369.9	380.1	480.1	511.7	534.2
<b>Ending Cash</b>	<b>0.4</b>	<b>156.0</b>	<b>212.4</b>	<b>256.2</b>	<b>254.5</b>	<b>328.6</b>	<b>392.6</b>	<b>641.3</b>	<b>1,011.1</b>	<b>1,391.2</b>	<b>1,871.4</b>	<b>2,383.1</b>	<b>2,917.3</b>

Sources: Oppenheimer &amp; Co. Inc. Estimates, Karyopharm Filings.

**Stock prices of other companies mentioned in this report (as of 7/3/2014):**

Agios (AGIO-NASDAQ, \$44.22, Not Covered)  
 Ambit (AMBI-NASDAQ, \$6.80, Not Covered)  
 Epizyme (EPZM-NASDAQ, \$34.24, Not Covered)  
 Sunesis (SNSS-NASDAQ, \$6.82, Not Covered)

## 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 substantial 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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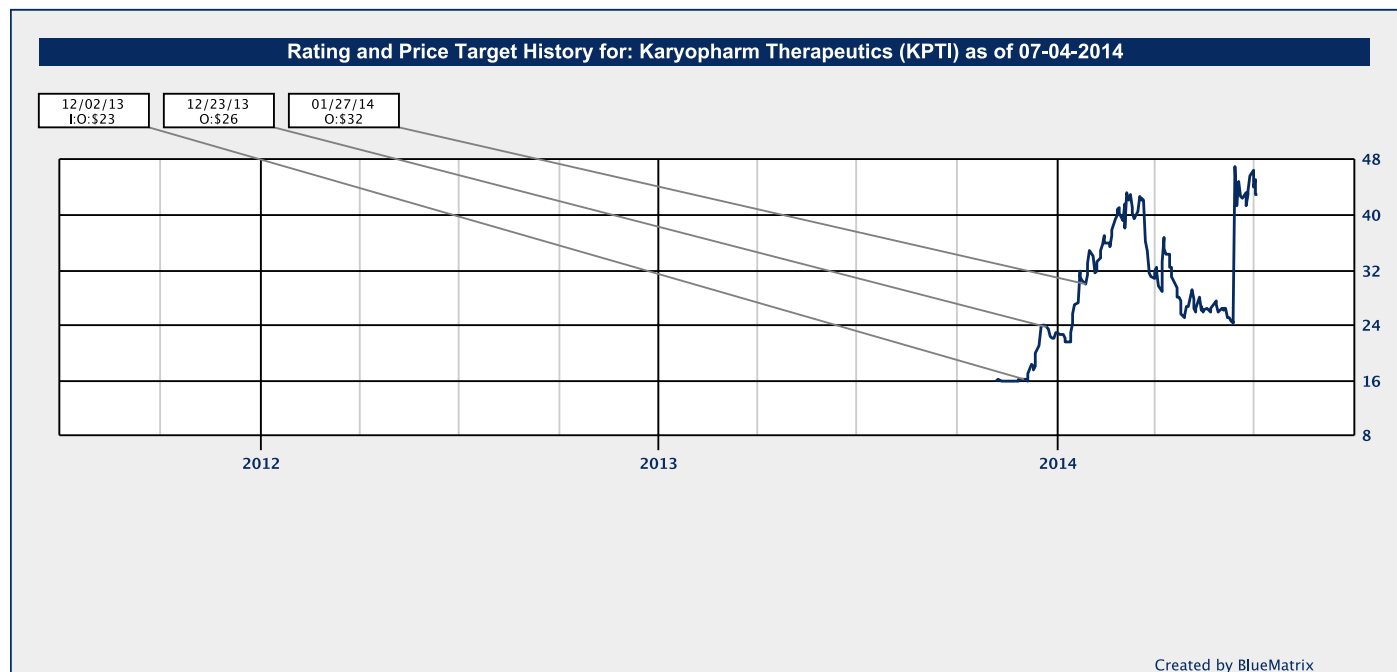
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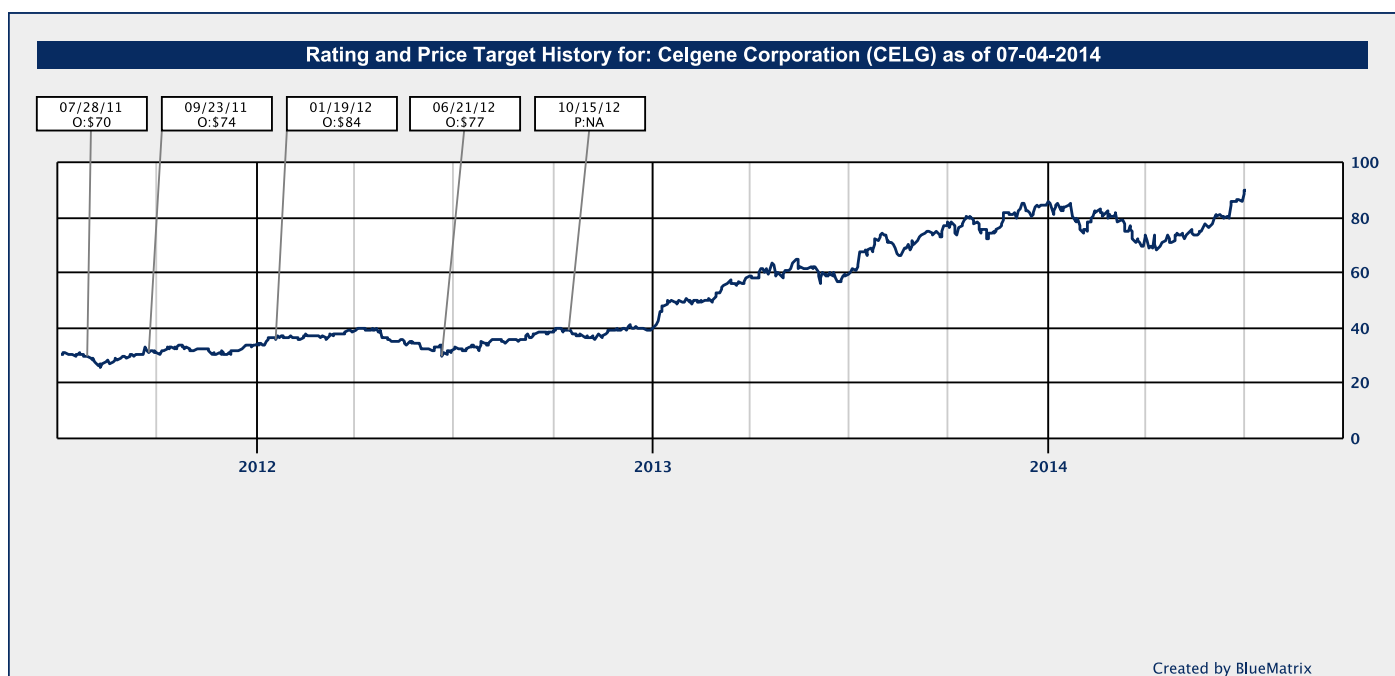
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		Percent			
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