December 2, 2013

HEALTHCARE/BIOTECHNOLOGY

Stock Rating:

OUTPERFORM

12-18 mo. Price Target	$23.00
KPTI - NASDAQ	$16.29
3-5 Yr. EPS Gr. Rate	71%
52-Wk Range	$19.09-$15.50
Shares Outstanding	28.7M
Float	8.1M
Market Capitalization	$468.0M
Avg. Daily Trading Volume	NA
Dividend/Div Yield	NM/NM
Book Value	$2.11
Fiscal Year Ends	Dec
2013E ROE	NA
LT Debt	$0.0M
Preferred	$0.0M
Common Equity	$459M
Convertible Available	No

Trading range since 11/6/13.

EPS Diluted	Q1	Q2	Q3	Q4	Year	Mult.
2012A	--	--	--	--	(2.71)	NM
2013E	(0.79)A	(0.85)A	(0.99)A	(0.60)	(3.06)	NM
2014E	(0.37)	(0.44)	(0.52)	(0.63)	(1.96)	NM

Revenue ($/mil)	Q1	Q2	Q3	Q4	Year	Mult.
2012A	--	--	--	--	0.6	NM
2013E	0.2A	0.2A	0.2A	0.2	0.8	NM
2014E	0.2	0.2	0.2	0.2	0.8	NM

Karyopharm Therapeutics

Novel Mechanism with Broad Applicability in Oncology; Initiating at Outperform

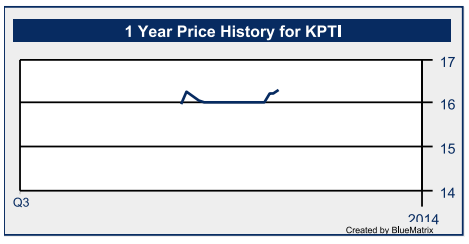
SUMMARY

Karyopharm Therapeutics (KPTI) is focused on the development of novel small-molecule therapeutics targeting the nuclear export protein XPO1. KPTI's lead asset Selinexor has demonstrated anti-cancer activity across a wide variety of cancer types. The company appears on track to initiate pivotal trials for three hematological malignancies in 1H14. Of the three, we believe Selinexor's greatest potential is in elderly acute myeloid leukemia (AML), a difficult-to-treat disease with few effective therapies available. Given its novel mechanism, we see broad potential for Selinexor across multiple cancer indications (including solid tumors), as well as potential for combination with other targeted therapies. We are initiating coverage with an Outperform rating, and a price target of $23.

KEY POINTS

- **Selective Inhibitors of Nuclear Export (SINE) platform has broad applicability**. By targeting XPO1, which is overexpressed in nearly all cancer types and is associated with resistance to chemotherapies, Selinexor has the potential to work across a broad range of hematological and solid cancers.
- **Greatest potential in elderly AML**. Selinexor has shown promising activity in heavily pretreated AML, with an acceptable safety profile when used with supportive care. Given the lack of new effective therapies for AML, particularly for elderly patients, we expect meaningful uptake of Selinexor in this setting.
- **Potential as salvage therapy in DLBCL and MM**. Preliminary data suggest efficacy in heavily pretreated patients failing all available therapies. We believe Selinexor will be used predominantly in patients failing multiple salvage therapies (e.g. after ibrutinib), and potentially in combination with other targeted therapies.
- **Potential in solid tumors**. To date, Selinexor has shown promising efficacy in solid tumor indications, again in heavily pretreated patients with highly refractory disease. We are encouraged by these preliminary results, and see potential in multiple indications, including colon, ovarian, and prostate cancer.
- **Initiating at $23 PT**. Our valuation contemplates Selinexor sales in elderly AML (peak $590M), r/r DLBCL (peak $360M), and r/r multiple myeloma (peak $350M), and probability-adjust each by 70%, 60%, and 60%, respectively. We do not factor in sales from solid tumor indications, suggesting potential for meaningful upside.

Stock Price Performance



Company Description

Karyopharm Therapeutics is a clinical-stage pharmaceutical company focused on discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases

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Investment Thesis

Karyopharm Therapeutics (KPTI) is a biopharmaceutical company focused on the development of novel, small molecule Selective Inhibitors of Nuclear Export (SINE) compounds that target the nuclear export protein XPO1. Karyopharm's lead asset is Selinexor (KPT-330), a SINE that is being examined in patients with heavily pretreated relapsed and/or refractory hematological and solid tumor malignancies. To date, Selinexor has demonstrated promising anti-cancer activity in patients who have failed all other available therapies and would otherwise have no treatment options left. We have highest conviction for Selinexor in elderly acute myeloid leukemia (AML), an indication with few available treatment options and a significant unmet need. We also see potential in refractory/resistant diffuse large B cell lymphoma (DLBCL) and multiple myeloma (MM), although intense competition from existing and investigational therapies will likely push Selinexor use to later lines of therapy (e.g. after failure of 4-5 regimens) initially. We are initiating coverage with an Outperform rating and a 12-18-month price target of $23.

SINE technology has broad potential across various oncology indications. Unlike other highly targeted oncology drugs that are only effective in specific malignancies or subsets of patients, SINEs have the potential to target a broad range of cancers. In preclinical studies, Karyopharm's SINE compounds have shown anti-cancer activity in both hematological and solid cancer models. In clinical studies, Selinexor has demonstrated anti-cancer activity even in the most refractory patients who have failed all available therapies. The novel mechanism makes Selinexor an attractive candidate for combination with other targeted agents to create even more potent treatment regimens.

In our view, Selinexor has the greatest potential in elderly acute myeloid leukemia (AML). With few effective treatment options available, particularly for elderly patients, AML is an indication with a significant unmet need. To date, Selinexor has shown promising activity in heavily pretreated AML patients. While adverse event (AE) rates are relatively high, AEs are generally mild-moderate and manageable with supportive care. Although the lack of effective therapies would normally suggest a lower bar for regulatory approval, we note that multiple agents in development for AML have been denied FDA approval in recent years due to lackluster efficacy. However, if Selinexor is able to demonstrate a favorable risk-benefit profile, we see great potential for Selinexor to transform the treatment paradigm for this particularly difficult indication.

Selinexor has promise as a salvage therapy in DLBCL and multiple myeloma. Interim Phase I data suggest efficacy in heavily pretreated patients with refractory and resistant diffuse large B cell lymphoma (DLBCL) and multiple myeloma (MM). However, several targeted therapies with promising activity are in development for both indications. For DLBCL, hematologists are most excited about Revlimid (lenalidomide) and Imbruvica (ibrutinib) in the salvage setting. For multiple myeloma, next generation proteasome inhibitors, histone deacetylase (HDAC) inhibitors, and targeted antibody therapies have gained the attention of hematologists. If approved, we believe Selinexor would be used predominantly in highly refractory, heavily pretreated patients after failing multiple lines of therapy (4-5) in the salvage setting.

Early-stage data also suggest activity in solid tumors. Karyopharm is examining Selinexor in a wide variety of solid cancers, including ovarian cancer and colorectal cancer. In Phase I studies, Selinexor has demonstrated efficacy in heavily pretreated patients who have failed all other available therapies. The company is still in the process of choosing specific indications for pivotal studies, but given the results to date, we believe Selinexor has broad potential in multiple solid tumor indications.

Management with a proven track record. We note that co-founder and CEO Michael Kauffman is a seasoned entrepreneur who brings extensive experience developing oncology drugs for similar indications. As Chief Medical Officer of Proteolix Inc., Dr. Kauffman led the development of Kyprolis for refractory myeloma; Proteolix was later acquired by Onyx Pharmaceuticals in 2009 where Dr. Kauffman became Chief Medical Officer. In addition, Dr. Kauffman played an active role in the development of Velcade at Millennium Pharmaceuticals. In addition, co-founder, CSO and President of R&D Sharon Shacham has previous experience at Epix Pharmaceuticals where she was a Senior Vice President of Drug Development.

Valuation. Our valuation currently contemplates sales from three indications: elderly AML, refractory/resistant DLCBL, and refractory/resistant multiple myeloma. We estimate peak sales of $590M, $360M, and $350M, respectively, in 2032. Given the efficacy results to date as well as the level of unmet need, we have highest conviction in the AML program, and probability-adjust our AML estimate by 70%. We probability-adjust our DLBCL and MM estimates by 60%. Because our model does not currently contemplate sales from additional indications, such as solid tumors and inflammation, we believe there is potential for substantial upside.

Pipeline

Drug Candidate / Indication	Preclinical	P1	P2	P2/3	Status/Anticipated
Selinexor (KPT-330) Advanced Hematological Malignancies					
Arm 1 (MM, WM, CLL, NHL)					Currently in dose escalation phase and enrolling fixed dose expansion cohort
Arm 2 (AML)					Currently in dose escalation phase; fixed dose expansion cohort expected to begin in Q4 2013
Arm 3 (T-Cell Lymphoma)					Currently enrolling
Advanced or Metastatic Solid Tumor Malignancies					Currently in dose escalation phase and enrolling fixed dose expansion cohort
Metastatic, locally advanced or locally recurrent soft tissue or bone sarcomas (food effect study)					Currently enrolling
Wound Healing (Topical Formulation) Topical Wounds					
KPT-350 & Related SINE Compounds Inflammation, Auto-Immune and Anti-Viral					
PAK4 Inhibitors Oncology					

• Verdinexor (KPT-335) is in a Phase 2b clinical trial for the treatment of pet dogs with newly-diagnosed or first relapse after chemotherapy lymphomas

Source: Company reports, www.karyopharm.com

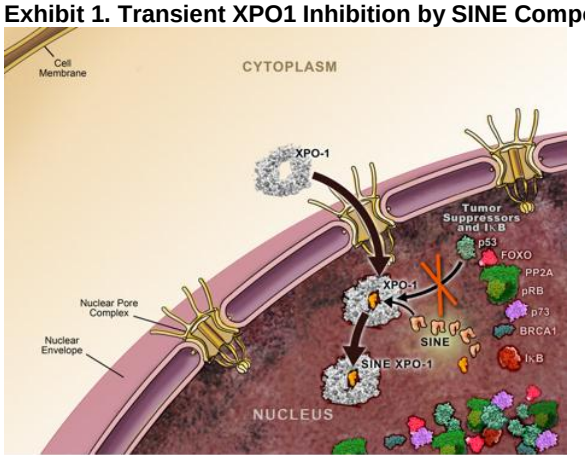
Selective Inhibitors of Nuclear Transport (SINE)

Cancer cells promote survival by suppressing nuclear export. In healthy cells, nuclear transport of proteins and other molecules is a highly regulated process that is mediated by specific carrier proteins. To date, seven nuclear export proteins have been identified, of which the most well-characterized is Exportin 1, or XPO1. XPO1 mediates the export of 220 cargo proteins, including the vast majority of tumor suppressor proteins, and importantly, is the sole exporter for most of these tumor suppressor proteins. XPO1 has been shown to be overexpressed in cancer cells. By increasing the export of tumor suppressor proteins from the nucleus, cancer cells are able to evade the natural apoptotic process, or programmed cell death, of genetically damaged cells.

SINEs inhibit nuclear export in cancer cells. Karyopharm's SINE (Selective Inhibitors of Nuclear Transport) compounds specifically inhibit XPO1, causing the nuclear accumulation of tumor suppressor proteins and thus apoptosis of cancer cells (Exhibit 1). Unlike other highly targeted oncology drugs that are only effective in specific malignancies or subsets of patients, SINEs have the potential to target a broad range of both hematological and solid tumor malignancies. Importantly, SINEs have minimal impact on

normal, non-cancerous cells, which have been shown in preclinical models to resume normal activity after transient XPO1 inhibition.

Exhibit 1. Transient XPO1 Inhibition by SINE Compounds



Source: Company reports, www.karyopharm.com

Potential for SINE use in inflammation and other indications. In addition to cancer, Karyopharm's SINE technology has potential applicability in additional non-cancer indications, including autoimmune and inflammatory diseases, wound healing, HIV and influenza. For example, XPO1 is responsible for the nuclear export of IκB in response to inflammation; blocking export of IκB allows nuclear IκB to bind NF-κB, blocking its inflammatory activity. XPO1 inhibition also causes nuclear accumulation of NF-κB inhibitors FOXO and COMMD1, leading to a multifaceted inhibition of NF-κB inflammatory activity.

Three SINEs in clinical development. Karyopharm's lead drug candidate is Selinexor (KPT-330), a wholly-owned, orally available small molecule inhibitor of XPO1. Selinexor is currently being investigated in Phase I human clinical trials in solid and hematologic cancers. Verdinexor (KPT-335), a SINE compound that is closely related to Selinexor, is in development for newly diagnosed or first time relapse lymphoma in dogs. Lastly, KPT-350, an oral SINE, is in preclinical development for inflammatory disease.

Selinexor (KPT-330) in Hematological Malignancies

Karyopharm's ongoing Phase I trial of Selinexor in advanced relapsed/refractory hematological malignancies is assessing patients who have received and failed multiple previous treatments. The majority of patients were elderly (>60 years old), with multiple comorbidities and on many other medications (often 5-10 different drugs). Karyopharm estimates that without effective therapy, the majority of these patients would progress within 4 weeks, shortly leading to death; any response or disease stabilization would thus be highly encouraging.

The open-label trial consists of three arms (Exhibit 2). Phase I results should help determine the Phase II clinical dose and dosing schedule, as well as provide efficacy data to support pivotal Ph. II/III trials for select indications.

Exhibit 2. Ph. I, Advanced Hematological Malignancies Trial Design

Arm	Cancer Type	N	KPT-330 Dosing	Primary Endpoint	Estimated Completion
Dose Escalation Phase:					
1	Chronic B-Cell Malignancies	60	Starting dose ranging from 3mg/m^2 to ≥30mg/m^2); 8-10 doses / 4-week cycle	AEs at 2 months and 12 months	Jan. 2016
2	Acute Myeloid Leukemia (AML)	40	Starting dose ranging from 3mg/m^2 to ≥30mg/m^2); 8-10 doses / 4-week cycle		
3	Peripheral (PTCL) and Cutaneous (CTCL) T Cell Lymphoma	12	30mg/m^2; 8 doses / 4-week cycle		
Fixed Dose Expansion Cohort:					
1	Multiple Myeloma (MM), Waldenstroms Macroglobulinemia (WM), Diffuse Large B-Cell Lymphoma (DLBCL)	25	35mg/m^2, 8 doses / 4-week cycle	AEs at 2 months and 12 months	Jan. 2016
2	Acute Myeloid Leukemia (AML)	25	40mg/m^2, 8 doses / 4-week cycle\		

Source: Company Reports

Interim results suggest efficacy across several NHL subtypes, including MM and DLBCL. To date, 49 patients have been enrolled in Arm 1, and 34 have been enrolled in Arm 2, as of September 2013; no patients in Arm 3 have been evaluated as of the September, 20, 2013 cutoff date. Based on interim results (Exhibit 3), Karyopharm intends to pursue pivotal studies for three initial indications: relapsed/refractory DLBCL, relapsed/refractory multiple myeloma, and relapsed/refractory elderly AML. Although Karyopharm is continuing to investigate Selinexor's potential in a multitude of indications, including Waldenstrom's macroglobulinemia (WM) and chronic lymphocytic leukemia (CLL), we focus our discussion below on the three indications in pivotal trials.

Exhibit 3. Ph. I, Arm 1 (Chronic B-Cell Malignancies) - Responses as of 9/20/13

	N	PRs + MRs	CR	PR	MR	SD	PD	WC	NE
MM	17	29%	-	6%	24%	41%	24%	6%	-
WM	2	100%	-	-	100%	-	-	-	-
CLL	5	60%	-	60%	-	40%	-	-	-
NHL			-						
DLBCL	5	20%	-	20%	-	40%	40%	-	-
MCL	3	33%	-	33%	-	33%	-	-	33%
FL	5	0%	-	-	-	100%	-	-	-
Transformed	2	0%	-	-	-	-	100%	-	-

Source: Karyopharm Prospectus (11/5/13)

Key for Responses:

CR: Complete Response
PR: Partial Response
MR: Minor Response
SD: Stable Disease
PD: Progressive Disease
WC: Withdrew Consent
NE: Non-Evaluable

Indication 1: Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL)

DLBCL is a common non-Hodgkin lymphoma. Diffuse large B cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL), accounting for nearly 30% of newly diagnosed NHL cases. DLBCL is an aggressive lymphoma that can develop de novo from germinal center B cells or activated B cells, or through transformation of low grade B cell lymphomas, such as CLL (this specific transformation is known as Richter's transformation), follicular lymphoma, or marginal zone lymphoma.

R-CHOP is the first-line standard of care for DLBCL; however, treatment options for relapsed/refractory DLBCL are limited. The majority of DLBCL patients (60-70%) present with advanced stage DLBCL. R-CHOP (rituximab in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone) is the current first-line standard of care for advanced stage DLCBL. However, over 50% of patients either relapse after or never respond to R-CHOP. Relapsed/refractory DLBCL patients are treated with second-line chemotherapy (either ICE or DHAP) and rituximab, and proceed to high-dose chemotherapy and autologous stem cell transplantation (ASCT) when possible. There are no effective therapeutic options for patients who are not candidates for ASCT and do not respond to second-line chemotherapy, and treatment for these patients is mostly palliative. However, the prognosis for all relapsed/refractory patients is generally poor, even for transplant-eligible patients. In younger patients with good organ function, R-

CHOP and transplantation lead to a cure rate of ~50%; older patients relapsing after initial chemotherapy and transplantation have an expected survival of less than one year.

Data support Selinexor use in refractory/resistant DLBCL. In preclinical cell line and mouse models, SINEs demonstrated activity across a variety of NHL subtypes. For DLBCL specifically, preclinical SINE candidate KPT-276 inhibited growth of DLBCL cells and induced p73 and Bax nuclear accumulation in p53-mutant DLBCL cell lines, suggesting restoration of apoptotic activity.

To date, Karyopharm has examined Selinexor in five refractory and heavily-pretreated DLBCL patients; one patient (20%) experienced a partial response, and two patients (40%) experienced disease stabilization (Exhibit 3). The patient who experienced a partial response is a 53-year old man who was refractory to primary therapy and transplant; the patient experienced a 93% response after 12 cycles of 6-12mg/m^2 Selinexor, with minimal side effects and a marked reduction in peripheral edema caused by his abdominal/pelvic tumor mass. As of September 2013, the patient is still on study, on Cycle 14.

Adverse event rates high but acceptable. In the entire Phase I, Arm 1 cohort, the most common adverse events were gastrointestinal adverse events and fatigue (Exhibit 4). Nausea, anorexia, vomiting, and diarrhea were all Grade 1 or 2 events, and according to Karyopharm, manageable with supportive care. Grade 2 fatigue was observed in 50% of patients, with one patient (3%) with Grade 3 fatigue. Neutropenia and thrombocytopenia were observed in 37% and 34% of patients, with 29% and 32% experiencing Grades 3 or 4 neutropenia or thrombocytopenia, respectively.

Exhibit 4. Select AE rates in Arm 1, as of 9/20/13

Adverse Event	Total	Grade 1/2	Grade 3/4
Nausea	79%	N/A	N/A
Anorexia	63%	N/A	N/A
Vomiting	39%	N/A	N/A
Diarrhea	39%	N/A	N/A
Fatigue	53%	50%	3%
Thrombocytopenia	34%	3%	32%
Neutropenia	37%	8%	29%

Note: AE rates were calculated based on 38 patients evaluated as of 9/20/13
Source: Karyopharm Prospectus (11/5/13)

While the frequency of GI AEs and fatigue is fairly high, our hematologist consultants are not overly concerned, as existing approved regimens already have a similar AE profile. Also, our consultants note that hematologists are used to dealing with neutropenia and thrombocytopenia on a regular basis, and thus would not be deterred by these AEs. However, given the overlapping AEs with existing regimens (e.g. R-CHOP), our consultants cautioned against using Selinexor in combination with these regimens; additional data will be necessary to confirm safety of combination regimens.

As of September 20, 2013, 49 serious adverse events (SAEs) occurred in 21 patients (55%) in Arm 1. According to the company, only one SAE, blurred vision, was attributed to Selinexor.

Hematologists find interim results encouraging, but additional data needed. While the clinical data are early stage and limited, we believe the occurrence of any response or disease stabilization is encouraging, given that these patients are highly refractory to standard therapies and would otherwise have no remaining options. However, our physician consultants would favor using other targeted agents in development for refractory/relapsed DLBCL, including Revlimid or ibrutinib, before resorting to Selinexor. They see potential for Selinexor's in combination regimens, due to its unique mechanism; however, they caution against using Selinexor in combination with R-CHOP because of overlapping AEs. Larger scale trials would be needed to better determine efficacy/safety in combination with existing and investigational regimens (see below).

Pivotal studies to begin 2014. Based on interim Ph.I results, KPTI intends to pursue an indication for relapsed DLBCL after chemotherapy and transplant, and plans to initiate a pivotal Phase II trial in 1H 2014. Karyopharm has also noted that, based on preclinical data suggesting synergies with other agents, the company hopes to initiate trials assessing Selinexor in combination regimens by year-end 2013.

However, DLBCL competitive landscape sets a high bar. While several agents are in development for relapsed/refractory DLBCL, our hematologist consultants are most excited about two targeted agents, Pharmacyclics's Imbruvica (ibrutinib, BTK inhibitor) and Celgene's Revlimid (lenalidomide), both of which have shown promising activity in clinical trials (Exhibit 5). We discuss the potential of both drugs, as well as Roche's obinutuzumab, in this indication below.

Exhibit 5. Select Late-Stage Investigational Therapies for Relapsed/Refractory DLBCL

Company	Drug	Mechanism	Status
Celgene	Revlimid	IMiD compound	Phase II
Pharmacyclics	Ibrutinib	BTK inhibitor	Phase II
Roche	Obinutuzumab	Anti-CD20 antibody	Phase II

Source: Company Reports

Exhibit 6. Revlimid: Response Rates in Relapsed/Refractory DLBCL

	Revlimid + Rituximab	Revlimid (single agent)
N	32	47
Median No. of Prior Therapies	3	4 (including ASCT)
ORR	28%	28%
CR	22%	11%
PR	6%	17%
SD	28%	26%
PD	37%	47%
NE	6%	0%
PFS	2.8 mo	2.7 mo
OS	10.2 mo	NA
DOR	NA	4.6 mo

Source: Wang et al. 2013, Vose et al. 2013

To date, Revlimid has shown promising activity in a subset of relapsed/refractory DLBCL patients. In Phase II trials of relapsed/refractory aggressive NHL (median of 4 prior experienced an ORR of 28% (11% CR/CRu, 17% PR; Exhibit 6). However, the median duration of response in these patients was only 4.6 months. Additionally, a separate retrospective study of patients treated with single-agent Revlimid in the salvage setting found that as patients with non-germinal center B-cell-like DLBCL respond well to Revlimid (53% ORR), whereas germinal center B-cell-like DLBCL patients responded poorly (9% ORR) (Exhibit 7). A Ph.II/III trial examining Revlimid vs. investigator's choice monotherapy in relapsed/refractory DLBCL patients who previously failed or were ineligible for transplant is ongoing. Patients in the trial will be risk-stratified according to germinal center B-cell-like vs. nongerminal B-cell-like subtype. Our hematologist consultants are excited about Revlimid's activity and are already using Revlimid in patients failing salvage chemotherapy and ASCT. However, given the lack of activity in the germinal center B-cell-like subtype, significant unmet need remains in the treatment of this patient population.

Exhibit 7. Response Rates to Single-Agent Revlimid by DLBCL Subtype

	All	GCB	Non-GCB
ORR	27.5%	8.7%	52.9%
CR	15.0%	4.3%	29.4%
PR	12.5%	4.3%	23.5%
SD	17.5%	30.4%	0.0%
PD	52.5%	60.9%	41.2%
Unknown	2.5%	0.0%	5.9%
Mean PFS	6.4 mo	3.3 mo	10.8 mo
Median PFS	2.6 mo	1.7 mo	6.2 mo

Source: Hernandez-Ilizaliturri et al, 2011

Similar to Revlimid, ibrutinib appears to be more active in non-germinal center B-cell-like DLBCL vs. the germinal center B-cell-like subtype (Exhibit 8). In an open-label Phase II study, patients with the non-germinal center B-cell-like subtype exhibited an ORR=41%, whereas germinal center B-cell-like subtype patients exhibited an ORR=5% (p=0.007); median OS was 9.7 months vs. 3.35 months for the two subtypes, respectively. As with Revlimid, our hematologist consultants are excited about ibrutinib's potential in the non-germinal center B-cell-like subtype, and would likely use either ibrutinib or Revlimid in relapsed/refractory patients with the appropriate phenotype. Thus, we believe Selinexor use would be restricted to non-germinal center B-cell-like DLCBL patients failing ibrutinib or Revlimid, or potentially in germinal center B-cell-like DLBCL patients after failing salvage chemotherapy and ASCT.

Exhibit 8. Response Rates to Single-Agent Ibrutinib by DLBCL Subtype

	GCB	Non-GCB
N	20	29
Median No. of Prior Therapies	3	3
ORR	5%	41%
CR	0%	17%
PR	5%	24%
Median OS	3.35 mo	9.7 mo

Source: PCYC EHA Presentation 2013

Lastly, Roche is also developing its humanized anti-CD20 antibody obinutuzumab (GA101, brand name: Gazyva) in the salvage DLBCL setting, prior to ASCT. In the Phase II GAUGUIN study, obinutuzumab showed single-agent activity in relapsed/refractory DLBCL prior to ASCT. Of the 10 patients evaluated (median of 4 prior therapies), end-of-treatment response was 28%, with 4% achieving CR/Cru. Median duration of response for all patients in the study (which also included MCL patients) was 9.8 months. However, our consultants do not see much utility in the salvage setting after R-CHOP, as they do not feel that obinutuzumab is sufficiently differentiated from rituximab, and would be reluctant to use obinutuzumab over Revlimid or another non-CD20-targeted drug.

$360M peak opportunity in the salvage setting post-ASCT and Revlimid/ibrutinib failure. We assume a prevalence of ~150K DLBCL patients in the US and ~240K in the EU; of these patients, we assume 50% will be refractory to front-line regimens and ASCT. Based on their superior clinical profiles in the salvage setting relative to other agents in development, as well as feedback from our hematologist consultants, we assume that Revlimid or Imbruvica will be used predominantly after front-line therapy and ASCT failure. However, because these agents are less effective in the germinal center B-cell-like patients. Assuming a price of $40,000/year (on par with Revlimid), we estimate peak sales of $363M in 2032 (Exhibit 9).

Exhibit 9. Oppenheimer Estimates – Selinexor Sales in Relapsed/Refractory DLBCL ($MM)

	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
US sales in R/R DLBCL	$8	$29	$43	$64	$81	$100	$107	$115	$123	$131	$140	$150	$160	$171	$183	$196	$126	$53	$41	$37
EU sales in R/R DLBCL	$17	$55	$76	$110	$131	$151	$152	$154	$156	$157	$159	$161	$162	$164	$166	$167	$107	$45	$35	$31
WW sales in R/R DLBCL	**$24**	**$84**	**$119**	**$175**	**$212**	**$251**	**$260**	**$269**	**$279**	**$289**	**$299**	**$311**	**$323**	**$335**	**$349**	**$363**	**$233**	**$98**	**$75**	**$68**

Source: Oppenheimer Estimates

Indication 2: Relapsed/Refractory Multiple Myeloma (MM)

For all multiple myeloma patients, relapse is inevitable. Multiple myeloma (MM) is characterized by the overproduction of malignant plasma cells that build up in the bone marrow. As a result, the myeloma cells crowd out normal blood-forming cells, causing anemia, leukopenia, and thrombocytopenia. MM is the second most common (10-15%) hematological malignancy that generally affects older patients; the median age of diagnosis is 70 years. The introduction of ASCT and the availability of agents such as Thalomid (thalidomide), Revlimid (lenalidomide), and Velcade (bortezomib) have helped extend overall survival in MM patients. In patients presenting at an age under 60 years, 10-year survival is approximately 30%. However, all patients eventually relapse and require salvage therapy.

Exhibit 10. Revlimid: Response Rates in Relapsed/Refractory Multiple Myeloma

	Study MM-009		Study MM-010	
	Rev/Dex	Pbo/Dex	Rev/Dex	Pbo/Dex
N	177	176	176	175
Median No. of Prior Therapies	2	2	2	2
ORR	61%	20%	60%	24%
CR	14%	1%	16%	3%
nCR	10%	1%	9%	2%
PR	37%	18%	36%	19%
SD	31%	58%	30%	55%
PD	3%	14%	2%	14%
NE	6%	8%	8%	6%

Pooled Survival Data (Long-Term Follow-Up)

	Rev/Dex	Pbo/Dex
Median TPP	13.4 mo	4.6 mo
Median DOR	15.8 mo	7.0 mo
Median PFS	11.1 mo	4.6 mo
Median OS	38.0 mo	31.6 mo

Source: Company Reports

Immunomodulatory compounds (IMiDs) and proteasome inhibitors typically used as both front-line and salvage therapy. Newly-diagnosed patients with symptomatic multiple myeloma are often treated with either Revlimid (lenalidomide, IMiD compound) or Velcade (bortezomib, proteasome inhibitor) in combination with dexamethasone; combination of all three in newly-diagnosed patients results in a 100% response rate, and is generally well tolerated, even in elderly patients. Patients who relapse after one to two years are often treated again with the same therapy. In contrast, patients who relapse after a shorter period of time receive a treatment with a different mechanism. For example, a patient relapsing on front-line Revlimid would receive Velcade second-line; however, a patient would not typically receive Thalomid (another IMiD) after failing Revlimid therapy. Other salvage therapy options include Pomalyst (IMiD) and Kyprolis (proteasome inhibitor); however, our hematologist consultants note that both agents have fairly low response rates in heavily pre-treated patients (median of 5 prior lines of therapy; Exhibit 11), and Kyprolis's cardiovascular and pulmonary AEs make it a less than ideal option.

Exhibit 11. Kyprolis and Pomalyst: Response Rates in Relapsed/Refractory Multiple Myeloma

	Kyprolis	Pomalyst + Dex
N	266	113
Median No. of Prior Therapies	5	5
ORR	22.9%	29.2%
CR	0.4%	0.9%
VGPR	4.9%	N/A
PR	17.7%	28.3%
Median DOR	7.8 mo	7.4 mo

Source: Company Reports

Clinical data, albeit limited, suggest Selinexor activity in MM. In Karyopharm's Phase I trial (Exhibit 3), of the 17 MM patients evaluated to date, 6% (1/17) achieved a partial response and 24% achieved a minor response. The one patient with a confirmed PR (85% reduction in free light chain) was refractory to all therapeutic classes, including Revlimid, Thalomid, Pomalyst, and Velcade, confirming Selinexor's activity in heavily pretreated patients. Although the data are still early-stage, based on the modest response rate, our consultants would still prefer to use other existing IMiDs and proteasome inhibitors in the salvage setting before resorting to Selinexor. However, they acknowledge that some minor response or disease stabilization is still better than disease progression and death, which would otherwise be the fate of these highly refractory patients. Lastly, our consultants are interested in the potential of combining Selinexor with dexamethasone and/or the aforementioned IMiDs and proteasome inhibitors, as long as there is no significant overlap in Aes. Safety of these combinations would need to be established in clinical trials, particularly in patients with other comorbidities (see below).

AE profile acceptable, although additional data in difficult-to-treat patients needed. Adverse event rates were pooled for all B-cell malignancies in Arm 1 and are discussed in the DLBCL section above. As with DLBCL, our hematologist consultants were generally not concerned about the high rates of GI AEs, fatigue, neutropenia, and thrombocytopenia, as they are comfortable managing them. However, our consultants note that multiple myeloma patients often suffer from renal impairment (both as a result of the disease as well as a side effect of lenalidomide use) as well as neuropathy (a side effect of Velcade use). Thus, to gain more comfort with Selinexor use in multiple myeloma, our consultants would require additional trial data in these difficult-to-treat patients.

Exhibit 12. Select Approved and Late-Stage Investigational Therapies for Relapsed/Refractory Multiple Myeloma

Company	Drug	Mechanism	Status
Celgene	Revlimid	IMiD compound	Approved
Celgene	Pomalyst	IMiD compound	Approved
Amgen/Onyx	Kyprolis	Proteasome inhibitor	Approved
Takeda	Velcade	Proteasome inhibitor	Approved
Takeda	MLN9708	Proteasome inhibitor	Phase III
Novartis	Panobinostat	HDAC inhibitor	Phase III
BMS	Elotuzumab	Anti-CS1 glycoprotein antibody	Phase III
JNJ/Genmab	Daratumumab	Anti-CD38 antibody	Phase II

Source: Company Reports

Developmental landscape for relapsed/refractory multiple myeloma has several promising candidates beyond Selinexor. Our consultants are particularly excited about two new antibody candidates in development for relapsed/refractory multiple myeloma: elotuzumab (anti-CS1 glycoprotein) and daratumumab (anti-CD38) (Exhibit 12). Our consultants are excited about the potential to combine these antibodies with Revlimid and other IMiDs, given their complementary immunomodulatory mechanisms. In addition, our consultants highlighted Takeda's oral proteasome inhibitor MLN9708, which they note would be a major advancement by allowing for the first all-oral therapy (MLN9708+Revlimid+dexamethasone) for multiple myeloma; Takeda is aiming for a late-2015 launch. Lastly, our consultants highlighted histone deacetylase (HDAC) inhibitor panobinostat (Novartis), which has demonstrated synergistic antitumor activity when combined with Velcade and dexamethasone. Importantly, the combination regimen was able to revert Velcade resistance in clinical trials. In the Phase II PANORAMA 2 study, panobinostat used in combination with Velcade and dexamethasone resulted in an ORR of 34.5% in heavily pretreated patients (median of four prior regimens) who had progressed on or within 60 days of the last Velcade-based therapy. However, despite achieving meaningful response rates, it is unclear whether the response rate will translate to a meaningful benefit in survival. We note that another HDAC inhibitor, vorinostat (Merck), led to an ORR of 56% (vs. 41% with placebo) when used in combination with Velcade and dexamethasone, but failed to produce a meaningful benefit in PFS (7.6 months vs. 6.8 months with placebo). Given the similar mechanism, it is unclear whether panobinostat's activity will translate to improved outcomes in terms of PFS in the ongoing Phase III trial.

$350M peak opportunity in the salvage setting after failing IMiDs and proteasome inhibitors. We assume a prevalence of ~70K multiple myeloma patients in the US and ~110K in the EU; of these patients, we assume that all will eventually progress after front-line regimens and ASCT. Given their superior response rates in the refractory setting, we assume that IMiDs (e.g. Revlimid) and proteasome inhibitors (e.g. Velcade) will be used predominantly in the salvage setting prior to Selinexor use. Assuming a price of $40,000/year (on par with Revlimid), we estimate peak sales of $348M in 2032 (Exhibit 13).

Exhibit 13. Oppenheimer Estimates – Selinexor Sales in Relapsed/Refractory Multiple Myeloma ($MM)

	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
US sales in R/R MM	$8	$16	$43	$73	$96	$121	$129	$137	$146	$156	$165	$176	$187	$199	$211	$225	$145	$61	$47	$43
EU sales in R/R MM	$10	$20	$49	$78	$97	$116	$117	$118	$118	$119	$120	$120	$121	$122	$122	$123	$79	$33	$25	$23
WW sales in R/R MM	**$18**	**$36**	**$92**	**$151**	**$193**	**$238**	**$246**	**$255**	**$265**	**$275**	**$285**	**$296**	**$308**	**$320**	**$334**	**$348**	**$223**	**$94**	**$72**	**$66**

Source: Oppenheimer Estimates

Indication 3: Relapsed/Refractory Elderly Acute Myeloid Leukemia (AML)

Few effective treatment options for AML, especially for elderly patients. Acute myeloid leukemia (AML) is characterized by the clonal proliferation of myeloid progenitor cells in the bone marrow and peripheral blood. The end result is the accumulation of

immature myeloid cells and myeloblasts, and the reduced production of normal red blood cells, platelets, and mature granulocytes. AML is the most common type of acute leukemia in adults, accounting for nearly 80% of cases, and is most common in older adults; the median age of diagnosis is 65 years.

For patients who are young and fit enough to withstand aggressive treatment, the current standard of care for AML usually consists of intensive induction chemotherapy (typically cytarabine, also known as AraC, followed by an anthracycline, such as daunorubicin or idarubicin), followed by consolidation chemotherapy and stem cell transplantation. However, for older patients with comorbidities, treatment options are limited, and outcomes are considerably worse. Of those who are given more intensive treatment, induction chemotherapy results in CR rates of 45–55%, and less than 10% of these patients survive for 5 years. However, many elderly AML patients cannot tolerate conventional induction chemotherapy, and are given attenuated treatment or supportive care only. Even if CR is achieved, the majority of AML patients eventually relapse.

Preclinical and clinical data support SINE use in AML. In preclinical studies, another SINE candidate KPT-185 demonstrated marked cytotoxicity against AML cell lines and primary AML blasts, inducing apoptosis, cell cycle arrest, and myeloid differentiation at submicromolar concentrations. KPT-185 was active against several different AML subtypes, including lines expressing mutations that are normally associated with poor prognoses (e.g. MLL-AF4, FLT3-ITD). Similarly, Selinexor caused potent cytotoxicity in leukemograft mouse models while sparing normal hematopoetic cells and prolonging overall survival.

Clinical data on Selinexor in AML patients are limited but encouraging. To date, 32 AML patients have been dosed with Selinexor (Exhibit 14), and as of September 20, 2013, three patients (9%) achieved complete remission, with two patients (6%) with complete blood count recovery and one patient (3%) with incomplete blood count recovery. 38% of patients achieved disease stabilization. Given that these are heavily pretreated and highly refractory patients, we view the occurrence of disease stabilization with limited cases of CR as encouraging. Our hematologist consultants agree that these interim results are promising; according to one consultant, an ORR+SD rate of 30% or above would be viewed as clinically meaningful.

Key for AML:

CR: Complete remission with complete blood count recovery
CR(i): Complete remission with incomplete blood count recovery
PR: Partial Remission
SD: Stable Disease
PD: Progressive Disease
WC: Withdrew Consent
NE: Non-Evaluable

Exhibit 14. Ph. I, Arm 2: AML Cohort – Responses as of 9/20/13

	N	CRs + CR(i)s	CR	CR(i)	SD	PD	WC	NE
AML	32	9%	6%	3%	38%	34%	1%	-

Source: Karyopharm Prospectus (11/5/13)

Safety profile acceptable with supportive care. Safety signals observed in the AML arm were generally similar to those observed in the chronic B-cell malignancy arm. Gastrointestinal AEs and fatigue were the most common types of AEs observed in the AML arm (Exhibit 15). As of September 30, the following GI-related SAEs were observed: nausea, anorexia, vomiting, and weight loss; all were generally Grade 1 or Grade 2 events (93%) and were responsive to standard supportive care. Fatigue was observed in 53% of patients, including two cases of Grade 3 fatigue (7%). However, physicians involved in Selinexor clinical trials noted that these AEs were manageable with supportive care.

Exhibit 15. Select AE Rates in Arm 2, as of 9/20/13

Adverse Event	Total	Grade 1/2	Grade 3/4
Nausea	60%	N/A	N/A
Anorexia	57%	N/A	N/A
Vomiting	40%	N/A	N/A
Weight Loss	23%	N/A	N/A
Fatigue	53%	47%	7%
Thrombocytopenia	N/A	N/A	10%
Neutropenia	N/A	N/A	7%

Note: AE rates were calculated based on 30 patients evaluated as of 9/20/13
Source: Karyopharm Prospectus (11/5/13)

Grade 4 thrombocytopenia (10%) and neutropenia (7%) were also observed, both thought to be related to advance disease and prior therapies. However, hematologists (both the clinical investigators involved in the Selinexor trials, as well as our consultants) were less concerned about these AEs as they are already common in AML patients and thus hematologists are already comfortable managing them.

Bar for AML is low, given lack of available options. Our hematologist consultants note that treatment regimens for AML have remained largely unchanged for the past 40 years. Thus there is a dire need for improved and effective therapeutics, especially for elderly patients who are unable to tolerate induction chemotherapy. Given the lack of effective therapies and few promising candidates in the pipeline, our consultants believe that the bar for uptake of a novel targeted therapy for AML is considerably lower than that for DLBCL and MM.

KPTI aiming for an initial indication in elderly AML. Karyopharm intends to aim for an indication in elderly AML refractory/resistant to front-line therapies. The company intends to initiate a pivotal Phase II trial in 1H14. In addition to response rates, our consultants will be paying close attention to transfusion independency and impact on quality of life as secondary endpoints.

Successful development of drugs for AML has historically been challenging. The AML developmental pipeline has often been referred to by the "Boulevard of Broken Dreams," as multiple drugs in development have failed to demonstrate sufficient efficacy for regulatory approval. Examples of failures in AML include tipifarnib, clofarabine, laromustine, and most recently, decitabine (brand name: Dacogen).

Exhibit 16. Select Approved and Late-Stage Investigational Therapies for AML

Company	Drug	Mechanism	Status	Indication
Eisai	Dacogen	DNA methyltransferase inhibitor	Approved (EU)	MDS; newly diagnosed elderly AML
Celgene	Vidaza	DNA methyltransferase inhibitor	Approved (EU)	AML with 20-30% blasts, not eligible for transplant
Boehringer Ingelheim	Volasertib*	Plk inhibitor	Phase III	Previously untreated elderly AML, ineligible for transplant
Sunesis	Vosaroxin	DNA topoisomerase II inhibitor	Phase III	R/R AML; Elderly AML (Cardiff trial)
Ambit	Quizartinib	FLT3 inhibitor	Phase II	FLT3-ITD(+) AML

**FDA Breakthrough Therapy Designation*
Source: Company Reports

Eisai's Dacogen is a DNA methyltransferase inhibitor approved for the treatment of myelodysplastic syndromes (MDS), a group of preleukemic disorders that have the potential to progress to AML. In 2012, Dacogen was approved by the EMA for newly diagnosed elderly AML patients (65 years and older) who are not candidates for induction chemotherapy. However, the FDA denied approval for the new indication, as the Oncologic Drugs Advisory Committee (ODAC) ruled that Dacogen failed to demonstrate a favorable risk-benefit profile in elderly AML. The pivotal trial failed to meet its primary endpoint of a statistically significant benefit in OS (7.7 months for the Dacogen arm vs. 5.0 months for the best supportive care arm; HR=0.85, p=0.108). ODAC members also expressed concern over other flaws with the trial, such as a lower response rate in the control arm than in previous trials, and the lack of improvement in patient-reported outcomes. Regardless of the FDA ruling, our hematologist consultants reported modest off-label use of Dacogen in elderly AML patients, solely because of the dearth of available options; however, given its questionable benefit, we do not view Dacogen as a meaningful competitor to any new approved targeted agent for AML.

However, the AML pipeline has several promising candidates, including one with FDA Breakthrough Therapy designation. Boehringer Ingelheim's Plk inhibitor volasertib has shown promising activity to date in patients ineligible for induction therapy. Results from a Phase II trial (reported at ASH 2012) show a vast improvement in patients receiving volasertib in combination with low-dose cytarabine (LDAC) vs. LDAC alone (ORR=31% vs. 13.3%); complete response rates were 16.7% and 6.7%, respectively. Common AEs observed in the combo arm were febrile neutropenia (50%), constipation (45.2%), nausea (40.5%), and anemia (40.5%). The FDA appears to have acknowledged volasertib's potential, granting it Breakthrough Therapy designation in September 2013. Boehringer Ingelheim initiated a Phase III study (POLO-AML-2) in patients 65 and older with previously untreated AML, ineligible for intensive remission induction therapy; results are expected in 2016.

Sunesis's topoisomerase II inhibitor vosaroxin has shown some promise in relapsed/refractory AML to date; the drug is currently in Phase III development in combination with cytarabine in relapsed and refractory AML, with OS results expected 1H14. In a Phase Ib/II trial of relapsed/refractory AML patients, vosaroxin was used in combination with AraC resulted in an ORR of 29% (CR=25%, CRp=3%, CRi=1%) and a

median OS of 6.9 months (vs. 3.4-5.9 months from historical data on other AML regimens). In a separate Phase II trial (REVEAL-1) focusing on elderly AML, patients dosed 72 mg/m2 of vosaroxin on days one and four experienced a median OS of 7.7 months, and a one-year survival rate of 38%. Although efficacy seemed promising, Sunesis decided not to proceed with development in this indication, due to the lack of an appropriate comparator arm. In a separate trial sponsored by Cardiff University, vosaroxin was examined both as monotherapy and in combination with AraC in a Phase II trial in front-line elderly AML; however, in March 2013, the trial's Data Monitoring and Ethics Committee (DMEC) recommended discontinuation of the monotherapy arm as it did not meet the pre-specified criteria for advancement. Data from the vosaroxin+AraC arm are expected 4Q13.

Celgene's DNA methyltransferase inhibitor Vidaza (azacitidine), which is approved for use in MDS and AML patients with up to 30% bone marrow blast, has also been examined in elderly AML. Although Vidaza is well tolerated by elderly patients, its efficacy in this subpopulation is questionable. In a recent single-center retrospective study, elderly patients treated with Vidaza achieved a similar OS as patients on intensive chemotherapy (1-year OS: 57% vs. 56%, p=0.93; 2-year OS: 35% versus 35%, p=0.92). However, Vidaza was better tolerated than intensive chemotherapy, resulting in fewer days spent in the hospital and fewer red blood cell and platelet transfusions. Our consultants also reported limited Vidaza use in elderly patients unable to tolerate induction chemotherapy, but would be most interested in combining Vidaza with other targeted therapies (e.g. Selinexor) to augment its effect.

Currently in Phase II development, Ambit's quizartinib (FLT3 and KIT inhibitor) targets the FLT3-ITD mutation, which is found in 30% of AML cases and is associated with a poor prognosis; patients bearing this mutation generally respond to induction therapy but relapse more quickly and at a higher rate. In a recent Phase II study (AC220-002), elderly FLT3-ITD(+) patients 60 years or older (of which 50% were refractory to their last therapy) exhibited a composite CR (CRc) rate of 57% and a median OS of 25.3 weeks (for patients aged ≥70 years, median OS was similar at 22.7 weeks). Remarkably, 16/110 (15%) of patients were alive for >12 months; half of these long-term survivors were aged ≥70 years. Ambit plans to initiate a Phase III study in adult relapsed/refractory FLT3-ITD(+) AML comparing quizartinib to salvage chemotherapy in early 2014. Our consultants find these results particularly encouraging, especially given the poor prognosis of these patients and the lack of available options.

Significant unmet need in elderly AML. Our hematologist consultants called the lack of new therapies for AML disappointing and demoralizing. While they understand the FDA's stringency in approving new therapies, they note that the goal of a new therapy is "not to hit a home run, but to get patients to the other end." Even with the large number of recent regulatory misses, our consultants believe that the bar for approval is still lower than that in other hematologic malignancies (e.g. DLBCL), given the huge unmet need and the lack of effective therapies.

$590M peak opportunity in elderly AML. We assume a prevalence of ~24K elderly (60+ year old) patients in the US and ~38K in the EU. Of these patients, we assume 80% will either fail or are ineligible for induction chemotherapy and transplant. Our consultant feedback indicates that physicians will continue to use Dacogen in this setting. Also, based on existing clinical data, we view volasertib as a highly promising candidate, and if approved, we envision this being used as well in elderly AML patients failing or ineligible for induction chemotherapy or transplant. Selinexor use would likely follow in patients failing Dacogen or volasertib. Assuming a 25% peak share in the salvage setting, and a price of $40,000/year (on par with Revlimid), we estimate peak sales of $592M in 2032 (Exhibit 17).

Exhibit 17. Oppenheimer Estimates – Selinexor Sales in Relapsed/Refractory AML ($MM)

	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
US sales in elderly AML	$34	$106	$150	$174	$200	$220	$232	$246	$260	$274	$290	$307	$324	$343	$362	$383	$246	$104	$80	$72
EU sales in elderly AML	$43	$128	$170	$186	$203	$210	$210	$210	$210	$210	$210	$210	$210	$210	$209	$209	$134	$57	$43	$39
WW sales in elderly AML	**$76**	**$234**	**$319**	**$360**	**$403**	**$430**	**$443**	**$456**	**$470**	**$484**	**$500**	**$516**	**$534**	**$552**	**$572**	**$592**	**$381**	**$160**	**$123**	**$112**

Source: Oppenheimer Estimates

Selinexor (KPT-330) in Solid Tumors

Karyopharm is also conducting an ongoing Phase I trial of Selinexor in advanced relapsed/refractory advanced solid tumors (Exhibit 18). As in the hematological malignancies trial, patients included in this trial are also heavily pretreated and have failed multiple lines of prior therapy. Phase I was designed to evaluate safety and to determine the Phase II clinical trial dose and dosing schedule; in addition, preliminary anti-cancer activity was observed in various solid malignancies. Although Karyopharm has not yet announced any pivotal trials for solid tumor indications, the promising anti-tumor activity observed to date suggests broad potential for Selinexor in solid tumors.

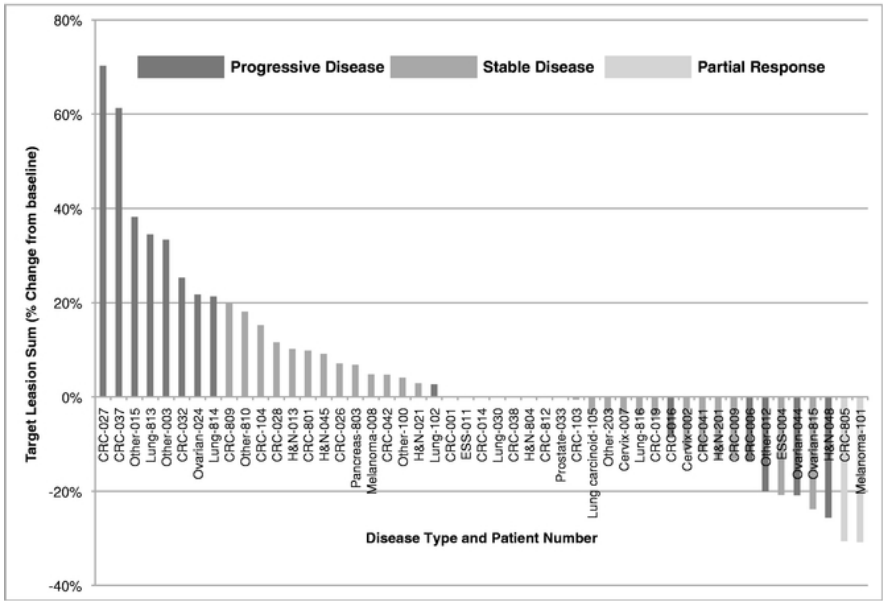
Exhibit 18. Phase I Interim Results: Selinexor in Advanced or Metastatic Solid Tumors - Responses as of Sept. 20th, 2013

	N	CR	PR	SD	PD	WC	NE
CRC	29	-	3%	34%	55%	-	7%
Head & Neck	9	-	-	44%	44%	-	11%
Lung	6	-	-	67%	33%	-	-
Ovarian	7	-	-	43%	29%	14%	14%
Cervical	2	-	-	100%	-	-	-
Endometrial Stromal Sarcoma	2	-	-	100%	-	-	-
Melanoma	2	-	50%	50%	-	-	-
Pancreas	5	-	-	20%	20%	40%	20%
Prostate	4	-	-	75%	-	25%	-
Other	10	-	-	30%	60%	-	10%
GBM	1	-	-	-	100%	-	-
Total	**77**	**0%**	**2%**	**43%**	**42%**	**5%**	**8%**

Source: Karyopharm Prospectus (11/5/13)

Patients evaluated to date received Selinexor doses ranging from 3 mg/m^2 to 50 mg/m^2, two to three times per week over each 28-day cycle. Response was evaluated in accordance with RECIST. To date, 2% of patients evaluated have experienced a PR, and 43% experienced disease stabilization. Given the progressive and highly refractory nature of disease in these patients, we view the occurrence of any response or disease stabilization as a positive indicator of anti-cancer activity. Changes in tumor size were also assessed in 49 patients (Exhibit 19). Based on Phase I results, Karyopharm will likely proceed with pivotal Phase II studies in select solid tumors.

Exhibit 19. Phase I Interim Results: Selinexor in Advanced or Metastatic Solid Tumors, Percentage Change in Tumor Size as of 9/20/13



Source: Karyopharm Prospectus (11/5/13)

Exhibit 20. Select AE Rates in Arm 3, as of 9/20/13

Adverse Event	Total	Grade 1/2	Grade 3/4
Nausea	81%	N/A	N/A
Anorexia	74%	N/A	N/A
Vomiting	60%	N/A	N/A
Dysgeusia	44%	N/A	N/A
Weight loss	40%	N/A	N/A
Diarrhea	31%	N/A	N/A
Fatigue	79%	65%	15%
Anemia	29%	21%	9%

Note: AE rates were calculated based on 68 patients evaluated as of 9/20/13
Source: Karyopharm Prospectus (11/5/13)

GI AEs and fatigue common but manageable. Common GI-related AEs included nausea, anorexia, vomiting, dysgeusia (distortion in the sense of taste), weight loss, and diarrhea (Exhibit 20). Fatigue was common in patients, with ten patients (15%) experiencing Grade 3 fatigue. Anemia was observed in 20 patients (29%), of which six patients (9%) experienced Grade 3 anemia. As of September 20, five patients (7%) have withdrawn from the trial due to AEs. The company notes that, although AE rates are high, they are for the most part manageable with supportive care; also, moving patients to a 2X/week dosing regimen has greatly improved AEs in patients.

Valuation

Our $23 price target is based on a DCF valuation using the WACC as the discount rate (15.21%) and a terminal growth rate of 2.0% on an estimated FCF of $48M in 2036 (Exhibit 21). Our cash flow estimates reflect sales for Selinexor in acute myeloid leukemia (AML), diffuse large B-cell lymphoma (DLBCL), and multiple myeloma (MM). We probability-adjust Selinexor sales in each indication by 70%, 60%, and 60%, respectively, given clinical results to date.

Exhibit 21. Karyopharm DCF Valuation

Cash Flow Analysis	
Revenue Growth (2014-2020)	NM
Revenue Growth (2020-2026)	7.1%
FCF Growth (2014-2020)	NM
FCF Growth (2020-2026)	1.0%
Terminal FCF Growth	2.0%
NPV FCF (2011-2025)	$655
Terminal FCF Value	$14
Total PV FCF	$670
Add Cash	$37
Less Debt	$0
Equity Value	$707
Shares Oustanding	31.1
DCF Share Value	**$22.72**
12 Month Fwd Value	**$22.72**

Source: Oppenheimer estimates.

Key Risks

Key risks to our target price include but are not limited to: 1) negative clinical or regulatory outcomes for key investigational product Selinexor in DLBCL, MM, elderly AML, and other oncology indications; 2) the emergence of significant new competition; and 3) lack of performance/trading history may cause share price volatility.

Management

Exhibit 22. Karyopharm Leadership

Officer	Title	Biography
Michael G. Kauffman M.D., Ph.D.	President, CEO, CMO, Director	Dr. Kauffman co-founded Karyopharm in 2008, and has served as President and CEO since Jan. 2011, CMO since Dec. 2012, and Director since 2008. Prior to Karyopharm, Dr. Kauffman was the CMO of Onyx Pharmaceuticals, where he led the development of Kyprolis for refractory myeloma. Prior to Onyx, Dr. Kauffman also served as an operating partner at Bessemer Venture Partners, President and CEO of Epix Pharmaceuticals. President and CEO of Predix

		Pharmaceuticals, and VP, Clinical at Millennium Pharmaceuticas. In addition, Dr. Kauffman has also held a number of senior positions at Biogen Idec. Dr. Kauffman currently serves on the board of directors for Verastem, Zalicus, and Metamark Genetics. Dr. Kauffman received his B.A. in Biochemistry from Amherst College, his M.D. and Ph.D. from Johns Hopkins Medical School, and trained in internal medicine and rheumatology at Beth Israel. He is board certified in internal medicine.
Sharon Shacham Ph.D., MBA.	CSO, President of R&D	Dr. Shacham co-founded Karyopharm in 2008, and has served as CSO and President of R&D since December 2012. Prior to Karyopharm, Dr. Shacham was the Senior VP of Drug Development at Epix Pharmaceuticals, and Director, Algorithm and Software Development at Predix Pharmaceuticals. Dr. Shacham received her B.Sc. in Chemistry, Ph.D. and M.B.A. from Tel Aviv University.
Paul Brannelly	Senior VP, Finance and Administration, Secretary, Treasurer	Mr. Brannelly joined Karyopharm in June 2013 as Senior VP, Finance and Administration, and has served as Secretary and Treasurer since July 2013. Prior to Karyopharm, Mr. Brannelly served as VP of Finance, CFO, Treasurer, and Secretary at Verastem. Prior to Verastem, Dr. Brannelly served as CFO of the Longwood Fund, and VP of Finance at Sirtris Pharmaceuticals. Dr. Brannelly has also held positions at Dyax Corporation and Zalicus Inc. Dr. Brannelly holds a Bachelors of Business Administration in Accounting from the University of Massachusetts at Amherst.
Dilara McCauley Ph.D.	VP, Product Leadership	Dr. McCauley serves as Karyopharm's Senior Director of Product Leadership, responsible for in vivo pharmacology, PK, toxicology, and canine oncology Dr. McCauley has over twelve years of experience in the biotechnology industry, with positions at Repigen Corporation, Epix and Predix Pharmaceuticals. Dr. McCauley holds a Ph.D. from the University of California, Santa Cruz.
Jamie Jamshidi	VP, Quality Assurance and Regulatory Affairs	Ms. Jamshidi brings over 26 years of industry experience, which includes 17 years at Amgen. After Amgen, Ms. Jamshidi founded the PQC Consulting, Inc., a consulting firm providing expert technical services, solutions, and training to pharmaceutical and biopharmaceutical companies. Ms. Jamshidi has extensive experience in the areas of product regulations, Quality Assurance, Manufacturing, Validation, Analytical Labs, Regulatory Submissions, Regulatory Inspections (PAI), Project Management, Managing Contract Manufacturing facilities, Technology Transfer and Team Leadership.
Robert Carlson Ph.D.	VP, Preclinical Development	Dr. Carlson joined Karyopharm in September 2013, bringing over 20 years of drug discovery and development experience. Prior to Karyopharm, Dr. Carlson was VP and Head of the Seattle site of JW Pharmaceuticals, VP and Head of Research at Myriad Genetics and the subsequent spinout Myrexis, and Director of Biology at Karo Bio. Dr. Carlson has also held positions at Bayer and Hoescht-Roussel. Dr. Carlson holds a B.S in Biochemistry from the University of Wisconsin-Madison and a Ph.D in Biochemistry from Brandeis University, and had postdoctoral training at the University of Michigan and Georgetown University.
Brian Austad Ph.D.	VP, Head of Pharmaceutical Sciences	Dr. Austad brings over 14 years of pharmaceutical experience, specializing in process chemistry with a focus on developing novel medicines for unmet needs. Prior to Karyopharm, Dr. Austad served as Sr. Advisor in Chemical Development at Rondaxe Pharma and as director of Process Chemistry at Infinity Pharmaceuticals. Dr. Austad has also held prior positions as a scientist and project leader at Eisai Research Institute. Dr. Austad holds a B.S. in Chemistry from the University of Wisconsin-Eau Claire and a Ph.D from the University of Wisconsin-Madison.
John McCartney Ph.D.	Senior Director, Product Leadership	Dr. McCartney brings over 20 years of drug development and project management experience. Prior to Karyopharm, Dr. McCartney held positions at GliaMed, EPIX Pharmaceuticals, Point Therapeutics, Cystic Fibrosis Foundation Therapeutics and Curis/Creative BioMolecules. Dr. McCartney holds a Ph.D. in Microbiology from Duke University, and completed postdoctoral training at the Massachusetts Institute of Technology.

Source: Karyopharm website

Other companies mentioned in this report as of 11/27/13:
Ambit (AMBI-NASDAQ, $12.50, Not Covered)
Boehringer Ingelheim (Private)
Bristol-Myers Squibb Co. (BMY-NYSE, $51.67, Not Covered)
Eisai Co., Ltd (4523-TYO, 3,990 JPY, Not Covered)
Genmab A/S (GEN-CPH, 229.40 DKK, Not Covered
GlaxoSmithKline (GSK-LON, 16.11 GBX, Not Covered)
Merck (MRK-NYSE, $49.83, Not Covered)
Novartis (NOVN-SWX, 71.20 CHF, Not Covered)
Johnson & Johnson (JNJ-NYSE, $94.98, Not Covered)
Pharmacyclics, Inc. (PCYC-NASDAQ, $124.00, Not Covered)
Roche Holding Ltd. (ROG-SWX, 252.20 CHF, Not Covered)
Sunesis Pharmaceuticals, Inc. (SNSS-NASDAQ, $5.10, Not Covered)
Takeda Pharmaceutical Company Ltd. (4502-TYO, 4950.00 JPY, Not Covered)

Karyopharm Income Statement ($MMs except per share data)

	2011	2012	1Q13	2Q13	3Q13	4Q13E	2013E	1Q14E	2Q14E	3Q14E	4Q14E	2014E
Selinexor Sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Contract & Grant Revenue	0.2	0.6	0.2	0.2	0.2	0.2	0.8	0.2	0.2	0.2	0.2	0.8
Total Revenue	**0.2**	**0.6**	**0.2**	**0.2**	**0.2**	**0.2**	**0.8**	**0.2**	**0.2**	**0.2**	**0.2**	**0.8**
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
R&D	8.6	14.1	5.4	5.6	6.0	6.5	23.5	8.0	10.0	12.0	15.0	45.0
SG&A	1.8	2.4	0.8	1.0	2.0	2.5	6.3	3.0	3.3	3.5	3.8	13.5
Operating Income	**(10.3)**	**(15.9)**	**(6.0)**	**(6.5)**	**(7.8)**	**(8.8)**	**(29.1)**	**(10.8)**	**(13.1)**	**(15.3)**	**(18.6)**	**(57.7)**
Interest Income	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.2	0.2	0.2	0.8
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
Pre-Tax Income	**(10.3)**	**(15.9)**	**(6.0)**	**(6.5)**	**(7.8)**	**(8.8)**	**(29.0)**	**(10.6)**	**(12.9)**	**(15.1)**	**(18.6)**	**(56.9)**
Tax Expense (Benefit)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tax Rate	NM	NM	NM	NM	0.0%	0.0%	NM	0.0%	0.0%	0.0%	0.0%	NM
Net Income (GAAP)	**(10.3)**	**(15.9)**	**(6.0)**	**(6.5)**	**(7.8)**	**(8.8)**	**(29.0)**	**(10.6)**	**(12.9)**	**(15.1)**	**(18.6)**	**(56.9)**
GAAP EPS	**($3.11)**	**($2.71)**	**($0.79)**	**($0.85)**	**($0.99)**	**($0.60)**	**($3.06)**	**($0.37)**	**($0.44)**	**($0.52)**	**($0.63)**	**($1.96)**
Avg. Shares Out. - Basic	3.3	5.9	7.6	7.6	7.8	14.7	9.5	28.7	28.9	29.1	29.3	29.0
Avg. Shares Out. - Diluted	3.3	5.9	7.6	7.6	7.8	15.3	9.6	30.5	30.7	30.9	31.1	30.8

Growth Analysis	**2011**	**2012**	**1Q13**	**2Q13**	**3Q13**	**4Q13E**	**2013E**	**1Q14E**	**2Q14E**	**3Q14E**	**4Q14E**	**2014E**
Total Revenue	**NM**	**NM**	NM	NM	NM	NM	**NM**	NM	NM	NM	NM	**NM**
COGS	**NM**	**NM**	NM	NM	NM	NM	**NM**	NM	NM	NM	NM	**NM**
R&D	**NM**	**NM**	NM	NM	NM	NM	**66.9%**	48.1%	77.8%	100.0%	130.8%	**91.3%**
SG&A	**NM**	**NM**	NM	NM	NM	NM	**160.3%**	275.0%	218.0%	75.0%	50.0%	**113.5%**
Operating Income	**NM**	**NM**	NM	NM	NM	NM	**83.0%**	NM	NM	NM	NM	**98.4%**
EPS	**NM**	**NM**	NM	NM	NM	NM	**82.4%**	NM	NM	NM	NM	**96.3%**

Source: Oppenheimer Estimates, Company Reports

Karyopharm Balance Sheet ($MMs)

	2011	2012	2013E	2014E	2015E
Assets					
Cash and Equivalents	6.5	0.4	118.8	37.0	66.9
Prepaid Expenses and Other Current Assets	0.4	0.6	0.4	0.8	4.1
Current Assets	**6.9**	**1.0**	**119.2**	**37.7**	**71.0**
Property, Plant, & Equipment	0.3	1.0	0.5	1.1	2.9
Deposits	0.0	0.3	0.0	0.0	0.0
Other	-	0.0	-	-	-
Total Assets	**7.2**	**2.3**	**119.6**	**38.8**	**73.9**
Liabilities					
Accounts Payables	1.1	1.1	1.4	2.8	5.2
Accrued Liabilities	0.8	0.8	0.9	1.9	4.1
Deferred Revenue	0.2	0.1	-	-	-
Other	0.0	0.0	-	-	-
Current Liabilities	**2.1**	**1.9**	**2.3**	**4.7**	**9.3**
Preferred Stock Subscription	7.0	9.0	-	-	-
Series A-2 Convertible Preferred	10.8	18.3	-	-	-
Series B Convertible Stock	-	-	-	-	-
Other Liabilities	-	-	-	-	-
Total Liabilities	**19.8**	**29.2**	**2.3**	**4.7**	**9.3**
Shareholders' Equity	**(12.6)**	**(26.9)**	**117.4**	**34.1**	**64.6**
Total Liabilities & Equity	**7.2**	**2.3**	**119.6**	**38.8**	**73.9**

Source: Oppenheimer Estimates, Company Reports

Karyopharm Statement of Cash Flows ($MMs)

	2011	2012	2013E	2014E	2015E
Net Income	(10.3)	(15.9)	(29.1)	(57.1)	(100.1)
Depreciation & Amortization	0.1	0.1	0.3	0.5	0.6
Share-Based Compensation	0.0	0.7	1.3	2.3	5.2
Other	-	-	-	-	-
Total Operating Sources	**(10.2)**	**(15.1)**	**(27.5)**	**(54.3)**	**(94.3)**
Prepaid Expenses and other current assets	(0.1)	(0.2)	0.2	(0.4)	(3.4)
Deposits	-	-	-	-	-
Accounts Payable	1.1	(0.1)	0.3	1.5	2.3
Accrued Expenses and other	0.4	0.0	0.1	1.0	2.2
Deferred Revenue	0.2	(0.1)	(0.1)	-	-
Other	-	-	-	-	-
Changes in Operating Assets/Liabilities	**1.7**	**(0.4)**	**0.6**	**2.0**	**1.2**
Operating Cash Flow	**(8.5)**	**(15.5)**	**(26.9)**	**(52.3)**	**(93.1)**
Capital Expenditures	(0.4)	(0.1)	(0.4)	(1.0)	(2.0)
Proceeds/Purchase of Securities	-	-	-	-	-
Other	-	-	-	-	-
Investing Cash Flow	**(0.4)**	**(0.1)**	**(0.4)**	**(1.0)**	**(2.0)**
Issuance/Purchase of Stock	0.0	0.0	117.2	-	125.0
Issuance/Payment Convertible Notes	-	-	-	-	-
Proceeds/Purchase of Preferred Stock	7.0	2.0		-	-
Proceeds/Purchase of Convertible Preferred	5.0	7.5		-	-
Other	-	-	-	-	-
Financing Cash Flow	**12.0**	**9.5**	**117.2**	**-**	**125.0**
Effect of Exchange Rates	-	-	-	-	-
Beginning Cash	3.4	6.5	0.4	90.2	37.0
Net Increase (Decrease) in Cash	3.1	(6.1)	89.9	(53.3)	29.9
Ending Cash	**6.5**	**0.4**	**90.2**	**37.0**	**66.9**

Source: Oppenheimer Estimates, Company Reports

Investment Thesis

Karyopharm is developing novel small-molecule Selective Inhibitors of Nuclear Export (SINE) compounds that target the nuclear export protein XPO1. Karyopharm's lead drug candidate is Selinexor (KPT-330), which is currently in Phase I development for advanced hematological and solid tumor malignancies. The company intends to initiate pivotal Phase II trials in elderly AML, relapsed/refractory DLBCL, and relapsed/refractory multiple myeloma. Early-stage data suggest anti-cancer activity in these indications. Based on its novel mechanism of action, we believe Selinexor has potential for broad applicability across multiple tumor types. We view KPTI as an attractive long-term investment and expect the stock to appreciate as additional clinical data in these and other cancer indications continue to emerge.

Price Target Calculation

Our 12-18-month price target of $23 is driven by a discounted cash flow analysis using a weighted average cost of capital (WACC) of 15.21% and a terminal growth rate of 2.0% on an estimated $48M of free cash flow in 2036.

Key Risks to Price Target

1) Negative clinical or regulatory outcomes for key investigational product Selinexor in DLBCL, MM, elderly AML, and other oncology indications; 2) the emergence of significant new competition; and 3) lack of performance/trading history may cause share price volatility.

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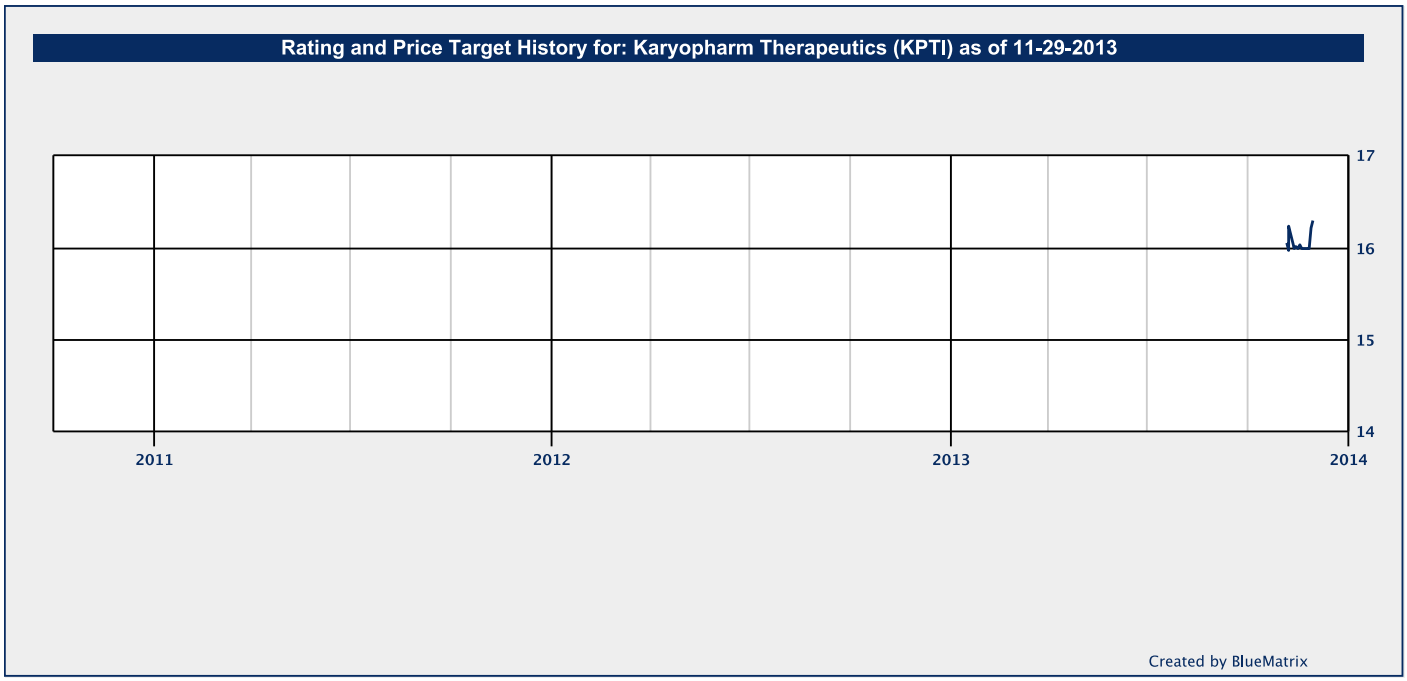
Stock Prices as of December 2, 2013

Amgen Inc. (AMGN - NASDAQ, $114.08, PERFORM)
Celgene Corporation (CELG - NASDAQ, $161.77, PERFORM)


Rating and Price Target History for: Karyopharm Therapeutics (KPTI) as of 11-29-2013
17
16
15
14
2011
2012
2013
2014
Created by BlueMatrix


Rating and Price Target History for: Amgen Inc. (AMGN) as of 11-29-2013
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04/20/11 O:$63
05/17/11 O:$66
02/08/12 P:NA
09/25/12 P:$85
10/24/12 P:$89
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07/31/13 P:$109
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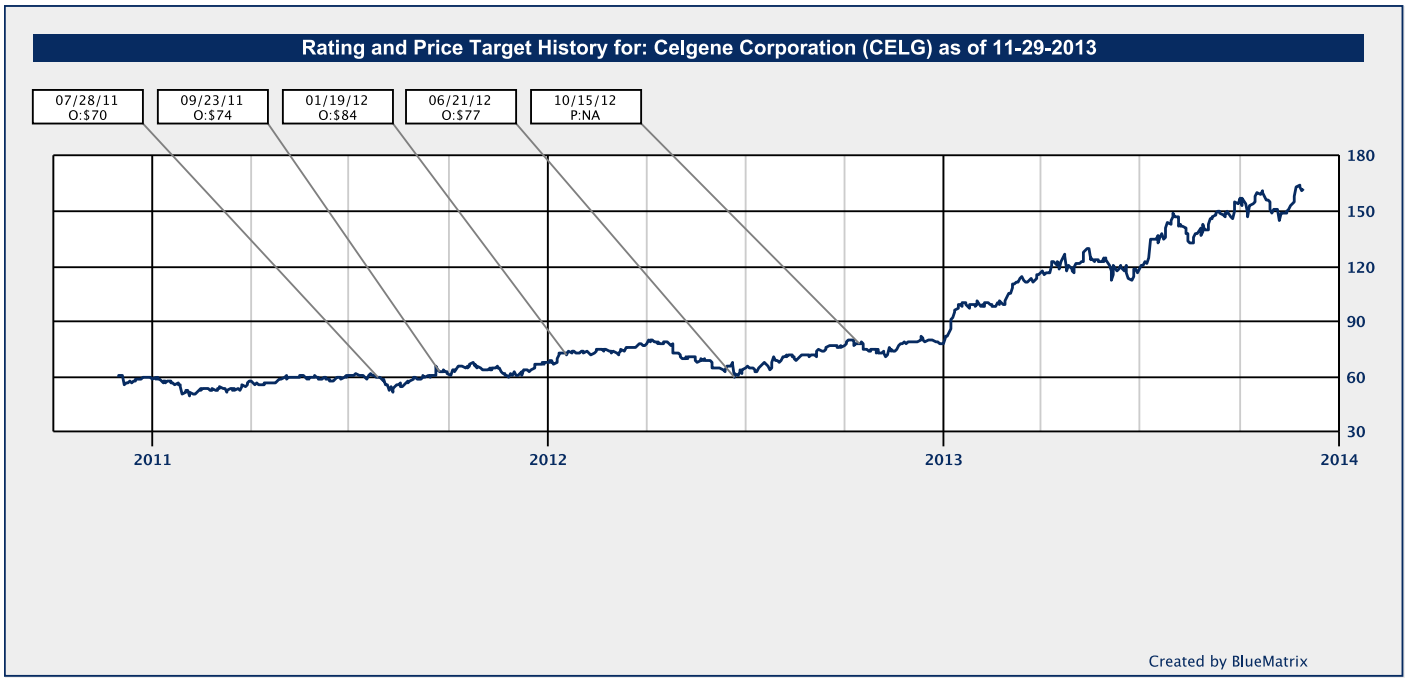
100
80
60
40
20
2011
2012
2013
2014
Created by BlueMatrix



All price targets displayed in the chart above are for a 12- to- 18-month period. Prior to March 30, 2004, Oppenheimer & Co. Inc. used 6-, 12-, 12- to 18-, and 12- to 24-month price targets and ranges. For more information about target price histories, please write to Oppenheimer & Co. Inc., 85 Broad Street, New York, NY 10004, Attention: Equity Research Department, Business Manager.

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Sell - anticipates that the shares will depreciate 10% or more in price within the next 12 months, due to fundamental weakness perceived in the company or for valuation reasons, or are expected to perform significantly worse than equities within the peer group.

Distribution of Ratings/IB Services Firmwide

			IB Serv/Past 12 Mos.	
Rating	Count	Percent	Count	Percent
OUTPERFORM [O]	293	49.24	140	47.78
PERFORM [P]	293	49.24	98	33.45
UNDERPERFORM [U]	9	1.51	4	44.44

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