Karyopharm Therapeutics Inc. (KPTI)

Initiating Coverage at Market Outperform with a $25 Price Target

MARKET OUTPERFORM | Price: $16.29 | Target Price: $25.00

MARKET DATA

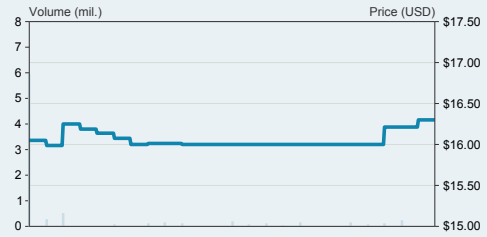
Price	$16.29
52-Week Range:	$15.50 - $19.09
Shares Out. (M):	27.6
Market Cap ($M):	$449.6
Average Daily Vol. (000):	231.0
Cash (M):	$153
Cash/Share:	$5.56
Enterprise Value (M):	$474
Float (M):	12.2
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2012A	2013E	2014E
Revenue ($M)	1Q	--	--	$0.0
	2Q	--	$0.4A	$0.0
	3Q	--	$0.0	$0.0
	4Q	--	$0.0	$0.0
	FY	**$0.6**	**$0.0**	**$0.0**
EPS	1Q	--	--	($0.30)
	2Q	--	($5.39)A	($0.35)
	3Q	--	($0.31)	($0.44)
	4Q	--	($0.29)	($0.55)
	FY	**($8.95)**	**($1.22)**	**($1.64)**

EPS 2013 Q2: Results are for six months ended June 30, 2013
Revenue ($M) 2013 Q2: Results are for six months ended June 30, 2013
Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE



INVESTMENT HIGHLIGHTS

We are initiating coverage of Karyopharm Therapeutics with a Market Outperform rating and a year-end 2014 $25 price target, based on the synthesis of our sum-of-the-parts NPV, standardized CAGR, and comparable company analyses. Karyopharm is an oncology-focused drug discovery and development company with a unique approach to the treatment of cancer with potentially far-reaching therapeutic impact. The company recently closed its initial public offering at $16 on November 12, 2013. Karyopharm's compounds target the cell's nuclear pore, specifically, proteins that chaperone genes in and out of the cell's nucleus whose role is to prevent a normal cell from transforming into a cancer cell. These genes are commonly referred to as oncogenes, and when they are aberrantly transported out of the nucleus and into the cytoplasm (the liquid portion of the cell's anatomy), they wreak havoc with the cell's normal programming, and transform the normal cell into one that is cancerous. KPTI's approach involves blocking these specific proteins, referred to as exportins (specifically, exportin-1, or XPO-1), so that they cannot pick up their designated "cargo". Thus, the targeted oncogene remains in the nucleus and the cell can then return to its normal state, differentiate, or die.

Compelling biology accompanies early evidence of clinical benefit. As investors well recognize, there are many elegant, biologic hypotheses for the treatment of cancer, often confounded by a lack of confirming clinical data. While we find the biologic theory behind KPTI's SINE approach attractive, the proof lies in the robust responses produced with the lead compound selinexor (KPT-330) in patients with a wide variety of tumor types, including 74% of whom showed CRs, PRs, or stable disease in advanced B-cell malignancies and who were progressing while on therapy (a meaningfully higher bar, in our view), CRs or SD in 47% of patients with relapsed/refractory AML, and 45% of patients with solid tumors showing a PR or SD. We remind investors that KPTI owns all worldwide rights to selinexor.

Man's best friend could be the investors' best friend as well. We highlight the fact that a closely related compound to selinexor, verdinexor (KPT-335), has produced impressive response rates in canine non-Hodgkin's lymphoma (NHL), a disease that closely mimics that of human NHL, which historically has served as a reliable surrogate for the development of drugs for NHL in humans. As of July 2013, verdinexor had produced an ORR of 34% and a disease control rate exceeding 90% in dogs. The degree of activity of verdinexor in dogs harkens back to that seen with ibrutinib (Imbruvica, PCYC, MO, $163 PT) in canines, which turned out to be predictive of the success seen in humans.

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History of significant value creation via successful drug development by founding CEO. Michael Kauffman, M.D., Ph.D., co-Founder and CEO, has two major drug approvals to his credit - Velcade and Kyprolis. Mainly as a result of the success that each of these drugs has had in the marketplace, Millennium Pharmaceuticals was acquired by the Japanese pharmaceutical company Takeda (JP-4502) in 2008 for $8.8 billion, while Onyx Pharmaceuticals was acquired by Amgen (AMGN, NC) for $10 billion in October 2013. Dr. Kauffman was a member of a small team that was responsible for the initial clinical development and registration strategy for Velcade, securing FDA approval in 2003 on the basis of a single-arm study in a relapsed/refractory myeloma patient population. Dr. Kauffman was also instrumental in the successful development and approval of Kyprolis, of which many on the Street were skeptical due to the perception that the FDA had raised the bar on drug approvals based on single-arm trials. Thus, much of our optimism regarding the successful development of the KPTI programs is based upon Dr. Kauffman's enviable track record in drug development.

Commencement of registration-directed trials during 2014 should catapult shares to the next level of valuation. In our view, when Karyopharm enters registration-directed trials next year, the valuation of the stock should be more reflective of other late-stage oncology companies steered by management teams that have successfully demonstrated significant value creation in the space. The "elite three" that we would compare KPTI to include Clovis Oncology (CLVS, NC), Puma Biotechnology (PBYI, NC), and Tesaro (TSRO, NC). While none of these companies is a perfect comparable for KPTI, we believe the shares belong amongst them based on the aforementioned factors.

INVESTMENT THESIS

We are initiating coverage of Karyopharm Therapeutics with a Market Outperform rating and $25 price target. Karyopharm is the first company that we are aware of that is seeking to capitalize on the concept of blocking the exit of oncogenes (genes whose function is to prevent a normal cell from transforming into cancer) from the nucleus into the cytoplasm. While this concept is not new (the now-defunct Kosan had a program in this area that was subsequently shuttered), Karyopharm is the first company to be able to develop nuclear export inhibitors with the appropriate pharmacologic properties to turn this class of agents into a real drug class. Previous agents in the category fell short in development because of poor safety, poor pharmacology, or both.

The company's lead program, selinexor (KPT-330) and its chemical cousin, verdinexor (KPT-335) for veterinary use, target a key nuclear export cargo protein alternatively referred to as XPO1 or CRM1 (for the purposes of this report, we shall herein refer to it as "XPO1"). Karyopharm refers to its drug candidates as SINEs, standing for selective inhibitor of nuclear export. These compounds exert profound anti-cancer effects as they interfere with the cancer cell's ability to export oncogenes (also referred to as tumor suppressors) out of the nucleus. This latter process renders the cell incapable of shutting itself down in the presence of DNA damage or other defects. Experiments have shown that the cancer cell increases its expression of XPO1, thus increasing the rate by which tumor suppressors are shuttled out of the nucleus; without "adult supervision", so to speak, the cell is able to replicate uncontrollably because it does not apoptose in response to cues that normally trigger such a reaction (e.g., irreparable DNA damage, increase in multiple chromosomes).

XPO1 turns out to be a particularly attractive target, as it appears to be the single cargo protein most responsible for handling the passage of oncogenes in and out of the nucleus. As stated above, Karyopharm is the first company we are aware of that has succeeded in the development of compounds that can block XPO1 with favorable drug-like properties that reach target inhibition at achievable doses, are well-tolerated, and show robust signs of clinical benefit in difficult-to-treat patients. As such, it has an inherent first-mover advantage in the space. Further, we believe value accrues to the company's pipeline for its discovery capabilities, as well as for the unique mechanism of action of the compounds.

The Karyopharm investment thesis would be incomplete without the mention of the role of the company's co-founder and CEO, Michael Kauffman, M.D., Ph.D. In our opinion, Dr. Kauffman should be credited with playing a major role in the development of two FDA-approved novel agents for the treatment of multiple myeloma, namely Velcade (bortezomib) and Kyprolis (carfilzomib). Dr. Kauffman was one member of a small team of executives at Millennium Pharmaceuticals (now part of Japanese pharmaceutical giant Takeda) responsible for the development and approval of Velcade for relapsed/refractory multiple myeloma.

In the development of this agent, Dr. Kauffman and the team at Millennium faced high odds - not only did the novel mechanism of action frighten a considerable number of scientists and clinicians (it was thought that inhibition of the proteasome could prove fatal), but the FDA clinical path of a single-arm, response rate-based trial was fraught with risk. The FDA granted accelerated approval to the drug in 2003 and many patients have benefited from Velcade therapy over the years. Subsequent to his tenure at Millennium, Dr. Kauffman became the Chairman of privately held Proteolix.

When carfilzomib (Kyprolis) encountered development hiccups, he was asked by the board to step in full time to right the program. Dr. Kauffman's involvement was critical to setting carfilzomib on the correct clinical and regulatory path which resulted in FDA approval of the drug in 2012. The company was subsequently acquired by Onyx for total consideration of roughly $700MM. It was the prospects for Kyprolis that ultimately led to the acquisition of Onyx by Amgen for $10 billion in October 2013. We have a high degree of confidence in Dr. Kauffman's ability to bring this same expertise to the development of the company's SINE portfolio.

FIGURE 1. Upcoming Milestones

Timing	Drug	Milestones
Dec 7-10	Selinexor	Updated Phase I and pre-clinical data presentations at ASH • Oral presentation of Phase I data in CLL and NHL (#30) • Oral presentation of XPO1 inhibition in AML (#237) • Oral presentation of preclinical efficacy in MM -/+ carfilzomib (#279) • Six poster presentations of pre-clinical and Phase I AML results (#1440, #1453, #1942, #3165, #3785, #3932,)
1H14	Selinexor	Initiation of first pivotal Phase II/III study in (elderly R/R AML, DLBCL, or MM)
1H14	Selinexor	Initiation of second pivotal Phase II/III study in (second potential indication)
1H14	Selinexor	Initiation of first Phase II trial in solid tumor indication (potentially gynecological malignancies)
1H14	Selinexor	Initiation of second Phase II trial in solid tumor indication (squamous cell cancer, e.g., head and neck, lung, or esophageal cancer)
2H14	KPT-350	IND completion for use in inflammation, auto-immune, and anti-viral indications
2H14	PAK Inhibitor	IND completion for use in oncology indications

Source: JMP Securities LLC and Company reports

VALUATION

We derive our year-end 2014 price target of $25 based on the synthesis of a discounted cash flow (DCF) analysis, a net present value assessment by a sum of the parts, and a relative valuation against a peer group of oncology-focused biotech companies (Figure 2).

FIGURE 2. Price Target Synthesis

Synthesis of Valuation Approaches	
Approach	**Valuation**
DCF Analysis	$ 22.07
SOTP	27.39
Comparables	26.03
Price Target	**$ 25.00**

Source: JMP Securities LLC and Company reports

Discounted Cash Flow Valuation

Our DCF valuation projects commercial sales of selinexor in the treatment of various hematologic malignancy indications in the U.S., as well as ex-U.S. associated royalties, while subtracting the cost of goods, projected operating expense, and tax. Net cash flows to the company are discounted to present values by 30% which, in our view, represents an appropriate risk-adjusted, discount factor for a Phase II-ready asset with demonstrated clinical activity. A terminal value for the company, calculated by applying a terminal growth rate of 2% to 2025 cash flow estimates, was similarly discounted to present day. Present values of free cash flows, together with the terminal value, were added to arrive at a residual value for the company, to which cash and long-term debt were added and subtracted, respectively. We thereby arrive at an equity valuation of $635MM. Dividing this amount by our estimated 2014 year-end outstanding share count of 28.8MM shares, we derive a per share valuation of $22.07. Our DCF assumptions are detailed further in Figure 3.

FIGURE 3. Discounted Cash Flow Valuation

Discounted Cash Flow Model	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Selinexor Revenue												
US Sales	-	-	18.4	86.3	262.2	515.9	848.8	1,199.0	1,447.5	1,617.3	1,688.9	1,759.7
Ex-US Royalties	-	-	-	4.6	12.2	35.8	70.4	120.6	170.4	206.1	228.5	240.6
Collaboration Revenue												
Total Revenues	**$ -**	**$ -**	**$ 18.4**	**$ 90.8**	**$ 274.3**	**$ 551.7**	**$ 919.2**	**$ 1,319.6**	**$ 1,617.8**	**$ 1,823.4**	**$ 1,917.3**	**$ 2,000.3**
Cost of product sales				7.8	21.0	41.3	67.9	95.9	115.8	129.4	135.1	140.8
COGS as % of revenue				*10%*	*11%*	*13%*	*14%*	*14%*	*14%*	*15%*	*15%*	*15%*
Gross Profit	0.0	0.0	18.4	83.1	253.4	510.4	851.3	1,223.7	1,502.0	1,694.0	1,782.2	1,859.5
R&D expense	38.1	47.6	78.6	106.1	118.8	128.3	134.7	141.5	148.5	156.0	168.5	176.9
R&D as a % of revenue				*117%*	*43%*	*23%*	*15%*	*11%*	*9%*	*9%*	*9%*	*9%*
SG&A expense	9.0	53.7	77.9	95.4	109.7	120.7	132.7	143.3	154.8	167.2	180.6	189.6
SG&A as a % of revenue				*105%*	*40%*	*22%*	*14%*	*11%*	*10%*	*9%*	*9%*	*9%*
Total operating expenses	47.1	101.3	156.4	201.5	228.5	249.0	267.5	284.8	303.4	323.2	349.0	366.5
% Margin				*222%*	*83%*	*45%*	*29%*	*22%*	*19%*	*18%*	*18%*	*18%*
Operating income (EBIT)	**(47.1)**	**(101.3)**	**(138.1)**	**(118.4)**	**24.8**	**261.5**	**583.8**	**938.9**	**1,198.7**	**1,370.8**	**1,433.2**	**1,493.1**
Taxes	0.0	0.0	(6.9)	(17.8)	5.0	65.4	204.3	328.6	419.5	479.8	501.6	522.6
Tax rate	*0%*	*0%*	*5%*	*15%*	*20%*	*25%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
After tax operating income	(47.1)	(101.3)	(131.2)	(100.6)	19.9	196.1	379.5	610.3	779.1	891.0	931.6	970.5
Discount year	0.00	1.00	2.00	3.00	4.00	5.00	6.00	7.00	8.00	9.00	10.00	11.00
Discount factor	1.0	1.3	1.7	2.2	2.9	3.7	4.8	6.3	8.2	10.6	13.8	17.9
PV	(47.1)	(77.9)	(77.6)	(45.8)	7.0	52.8	78.6	97.3	95.5	84.0	67.6	54.2

Residual value of cash flow	$482	**Terminal Value**	193.4
+Cash and Cash equivalents	153		
Company value	635		
-Long-term debt on 12/31/13	0		
Value of equity	$635		
Fully diluted shares outstanding on 12/31/14	28.78		
Price/share	**$22.07**		
Discount Rate	30.0%		
Terminal growth rate	2%		

Source: JMP Securities LLC and Company reports

Sum-of-the-Parts Valuation

In valuing KPTI shares based on a sum-of-the-parts (SOTP) analysis, we projected selinexor revenues per anticipated approved indications of DLBLC, AML, and MM in both domestic and royalty territories. For U.S. sales, we applied increasing contribution margins plateauing at 40% to arrive at projected net income within each indication. For the royalty territories, we applied a 100% contribution margin to an estimated straight-line royalty of 15%. Projected U.S. net income and ex-U.S. royalty revenue were discounted to present values using a discount rate of 30%. Meanwhile, terminal values for each of the potential income streams were determined by applying a long-term growth rate of 2%.

In DLBCL, our model estimates selinexor revenues approaching ~$800MM in 2025, contributing to a present valuation of $313MM, or $10.87 per share. Similarly in AML, we derive a present valuation of $160, or $5.56 per share. Finally, we model ~$630 peak sales from salvage use in treatment of multiple myeloma, arriving at an incremental present valuation of $161MM, equivalent to $5.63 per share. Adding cash on hand of $5.33 per share, we arrive at an SOTP valuation of $27.39. Our SOTP valuation, together with revenue and our contribution modeling assumption, is detailed in Figure 4.

FIGURE 4. Sum-of-the-Parts Valuation

NPV Sum of the Parts	WW	US	Ex-US
Selinexor AML	**$ 5.56**	$ 4.01	$ 1.55
Selinexor DLBCL	**$ 10.87**	$ 8.16	$ 2.71
Selinexor MM	**$ 5.63**	$ 4.66	$ 0.96
Cash and Equivs on Hand	**$ 5.33**		
Total NPV	**$ 27.39**	**$ 16.84**	**$ 5.22**

Selinexor AML, NPV	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
US Sales ($MM)				$ 18	$ 58	$ 99	$ 150	$ 213	$ 254	$ 288	$ 299	$ 311	$ 323
Contribution Margin				*5%*	*10%*	*18%*	*25%*	*32%*	*37%*	*40%*	*40%*	*40%*	*40%*
Operating Margin					**5.8**	**17.8**	**37.4**	**68.3**	**94.0**	**115.2**	**119.8**	**124.5**	**129.4**
Terminal Value													**462.0**
Discount Period					3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
PV of CF to KPTI					**2.7**	**6.2**	**10.1**	**14.1**	**15.0**	**14.1**	**11.3**	**9.0**	**33.0**
Discount Rate	30%												
Terminal Growth	2%												
NPV	**$ 115.52**												
# Shares outstanding (mm)	28.8												
Incremental price per share	**$ 4.01**												
Ex-US Sales ($MM)					$ 30	$ 62	$ 112	$ 164	$ 236	$ 282	$ 319	$ 334	$ 349
Royalty rate						*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
Royalty to Karyopharm						**9.3**	**16.7**	**24.7**	**35.4**	**42.3**	**47.9**	**50.1**	**52.4**
Terminal Value													**174.7**
Discount Period					3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
PV of CF to KPTI						**3.3**	**4.5**	**5.1**	**5.6**	**5.2**	**4.5**	**3.6**	**12.7**
Discount Rate	30%												
Terminal Growth	0%												
NPV	**$ 44.53**												
# Shares outstanding (mm)	28.8												
Incremental price per share	**$ 1.55**												

Selinexor DLBCL, NPV	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
US Sales ($MM)					$ 6	$ 69	$ 186	$ 356	$ 528	$ 630	$ 738	$ 771	$ 802
Contribution Margin					*10%*	*18%*	*25%*	*32%*	*37%*	*40%*	*40%*	*40%*	*40%*
Operating Margin					**0.6**	**12.4**	**46.5**	**114.0**	**195.5**	**251.9**	**295.0**	**308.4**	**320.8**
Terminal Value													**1,145.8**
Discount Period					3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
PV of CF to KPTI					**0.3**	**4.3**	**12.5**	**23.6**	**31.2**	**30.9**	**27.8**	**22.4**	**81.8**
Discount Rate	30%												
Terminal Growth	2%												
NPV	**$ 234.81**												
# Shares outstanding (mm)	28.8												
Incremental price per share	**$ 8.16**												
Ex-US Sales ($MM)						$ 6	$ 74	$ 197	$ 370	$ 564	$ 684	$ 803	$ 854
Royalty rate						*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
Royalty to Karyopharm						**0.9**	**11.2**	**29.5**	**55.4**	**84.6**	**102.6**	**120.4**	**128.1**
Terminal Value													**426.9**
Discount Period						4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
PV of CF to KPTI						**0.3**	**3.0**	**6.1**	**8.8**	**10.4**	**9.7**	**8.7**	**31.0**
Discount Rate	30%												
Terminal Growth	0%												
NPV	**$ 78.04**												
# Shares outstanding (mm)	28.8												
Incremental price per share	**$ 2.71**												

Selinexor MM, NPV	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
US Sales ($MM)					$ 22	$ 95	$ 180	$ 279	$ 417	$ 530	$ 580	$ 607	$ 634
Contribution Margin					*10%*	*18%*	*25%*	*32%*	*37%*	*40%*	*40%*	*40%*	*40%*
Operating Margin					**2.2**	**17.0**	**45.0**	**89.3**	**154.1**	**211.8**	**232.2**	**242.7**	**253.7**
Terminal Value													**768.9**
Discount Period					3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
PV of CF to KPTI					**0.9**	**5.1**	**10.0**	**14.8**	**18.9**	**19.2**	**15.6**	**12.1**	**37.7**
Discount Rate	35%												
Terminal Growth	2%												
NPV	**$ 134.23**												
# Shares outstanding (mm)	28.8												
Incremental price per share	**$ 4.66**												
Ex-US Sales ($MM)						$ 13	$ 53	$ 108	$ 198	$ 290	$ 370	$ 386	$ 401
Royalty rate						*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
Royalty to Karyopharm						**1.9**	**7.9**	**16.2**	**29.7**	**43.5**	**55.6**	**58.0**	**60.1**
Terminal Value													**171.7**
Discount Period						4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
PV of CF to KPTI						**0.6**	**1.8**	**2.7**	**3.6**	**3.9**	**3.7**	**2.9**	**8.5**
Discount Rate	35%												
Terminal Growth	0%												
NPV	**$ 27.75**												
# Shares outstanding (mm)	28.8												
Incremental price per share	**$ 0.96**												

Source: JMP Securities LLC and Company reports

Comparable Company Analysis

Finally, we sought to value KPTI shares relative to a select peer group of oncology-focused biotechnology companies with assets in development (Figure 5). Relative to the group mean market cap valuation, we derive a per share valuation of ~$26 for KPTI shares.

FIGURE 5. Comparable Company Valuation

Comparable	Ticker	Price	Market Cap	Cash	Debt	EV
Acceleron Pharma Inc	XLRN	$21.77	$611	$40	$18	$590
Ambit Biosciences Corp	AMBI	$12.55	$224	$17	$0	$207
Array Biopharma Inc	ARRY	$5.72	$707	$61	$99	$746
Clovis Oncology Inc	CLVS	$60.29	$1,819	$144	$0	$1,675
Cell Therapeutics Inc	CTIC	$1.94	$252	$50	$5	$206
Cyclacel Pharmaceuticals Inc	CYCC	$4.83	$90	$34	$0	$56
Endocyte Inc	ECYT	$11.54	$417	$34	$0	$383
Epizyme Inc	EPZM	$20.94	$595	$98	$0	$497
Exelixis	EXEL	$5.83	$1,074	$170	$323	$1,226
Infinity Pharmaceuticals Inc	INFI	$14.61	$703	$176	$0	$527
Oncomed Pharmaceuticals Inc	OMED	$13.46	$376	$16	$0	$359
Puma Biotechnology Inc	PBYI	$49.79	$1,428	$137	$0	$1,291
Sunesis Pharmaceuticals Inc	SNSS	$5.05	$273	$15	$18	$275
Stemline Therapeutics Inc	STML	$20.66	$267	$2	$2	$267
TESARO Inc	TSRO	$39.00	$1,277	$125	$0	$1,151
Average			**$674**			**$630**
Karyopharm Therapeutics Inc	KPTI	$16.29	$450	$0	$0	$449

Comparable Valuation	$26.03

Source: JMP Securities LLC and Company reports

INVESTMENT RISKS

Clinical. Drug development is an inherently risky business. Clinical trials always carry a risk of failure and Karyopharm's assets (Selinexor (KPT330), KPT-350, PAK4 inhibitor, verdinexor, or future drug candidates) may fail to demonstrate meaningful levels of efficacy in current or future clinical trials.

Regulatory and commercial. The ability of Karyopharm to market its drugs depends on those drugs obtaining approval from the FDA and foreign regulatory agencies. Failure to achieve approval or delays in the timelines to approval could negatively impact the company's share price.

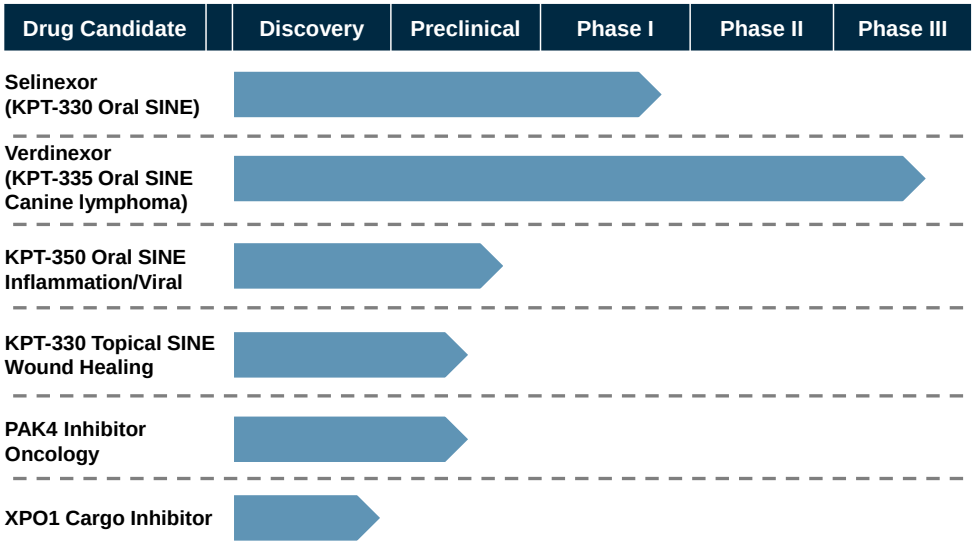
Competitive. Hematologic malignancies including multiple myeloma, indolent non-Hodgkin lymphoma and acute myeloid leukemia represent increasingly competitive fields and Karyopharm faces competition from both commercial and development-stage companies with product(s) or product candidates addressing similar clinical indications. Some of these companies may possess substantially greater R&D and commercial resources than Karyopharm. As such, there is no assurance Karyopharm will be competitive or differentiated from other drug products.

Financial. Following its IPO, we estimate that Karyopharm will end 4Q13 with approximately $153MM in cash and cash equivalents, which should be adequate resources to fund operations into 2015, according to Karyopharm financial guidance. We anticipate that the company is likely to seek additional equity financing in the form of a secondary offering in order to complete the development of its drug candidates, creating dilution risk for existing shareholders.

COMPANY OVERVIEW

Karyopharm Therapeutics (KPTI) is a Natick, MA based, clinical-stage, biopharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitors of Nuclear Export (SINE) compounds function by preventing the export of tumor suppressor proteins from the nucleus, driving their accumulation and restoration of function. The company's lead pipeline candidate selinexor (KPT-330) is a Phase I orally available small molecule inhibitor of XPO1, set to initiate pivotal Phase II/III evaluation in various hematologic malignancies in 2014. Karyopharm is also developing selinexor and SINE as potential therapies for autoimmune and inflammatory disease, viral infections and wound healing.

FIGURE 6. Karyopharm Development Pipeline



Source: JMP Securities LLC and Company reports

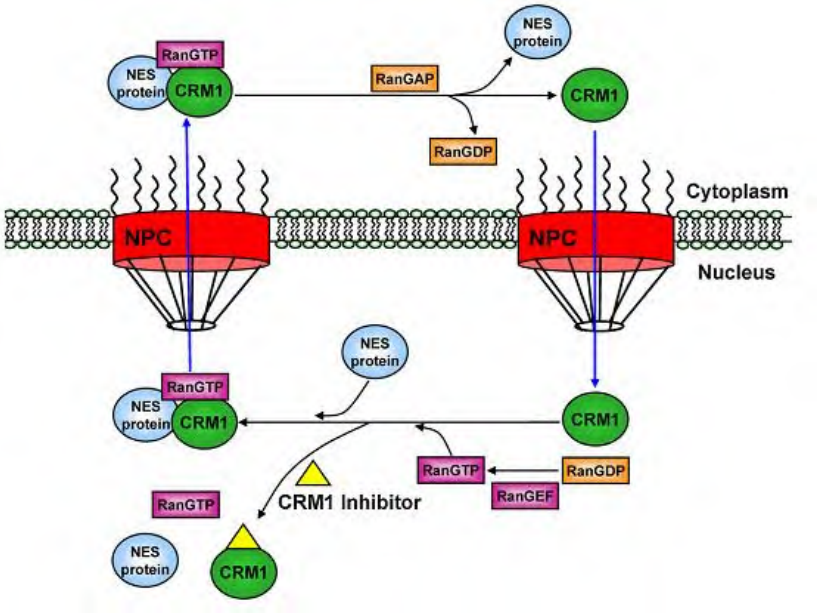
SELINEXOR – A NEW SINE OF HOPE IN THE TREATMENT OF CANCER

As highlighted above, the Karyopharm development platform leverages unparalleled pioneering work in the characterization of nuclear pore complex machinery and trafficking of tumor suppressor proteins to and from the surrounding cytoplasm. The company's SINE discovery platform was founded internally, principally driven through the efforts of scientific co-Founder and Chief Scientific Officer, Dr. Sharon Shacham. Selinexor (KPT-330), an inhibitor of the nuclear transport protein Exportin 1 (XPO1), is currently being evaluated in multiple Phase I/II clinical trials for patients with both hematological and solid tumor malignancies. Inhibition of XPO1 (one of seven nuclear export proteins) reduces transport of over 285 proteins and protein RNA complexes from the nucleus to the cytoplasm. XPO1 aids in the export of proteins that carry a leucine-rich, hydrophobic nuclear export sequence (NES), which includes many proteins necessary for progression to malignant disease. Naturally occurring, irreversible XPO1 antagonists such as leptomycin B (LMB) exist, but have proven toxic in both pre-clinical models and in the clinic. Selinexor, an orally available small molecule, is a potent, selective inhibitor of XPO1 mediated nuclear export, and has been engineered by Karyopharm to have significant activity against cancer cells over-expressing XPO1, while being safe enough to be well tolerated by healthy cells and tissue.

Nuclear Export Inhibition as a Mechanism of Anticancer Therapy

The nuclear transport protein XPO1, also called chromosome region maintenance 1 (CRM1), is known to be overexpressed two- to four-fold in many tumor types, and to promote evasion of apoptosis and resistance to chemotherapy (Turner J, et al., *Biochem Pharmacol*, 2012). XPO1 overexpression promotes these maladaptive effects through cytoplasmic mis-localization of multiple tumor suppressor proteins (Lapalombella, R, et al., *Blood*, 2012). Small proteins (less than 40 to 65 kDa) can cross the nuclear membrane in a passive manner; however, larger proteins require the assistance of transport molecules called karyopherins. The nuclear to cytoplasmic transport of proteins and RNA complexes is a highly coordinated mechanism, and XPO1, a type of karyopherin, is able to transport both RNA and proteins mediated by a GTPase activating protein (Figure 7). In healthy cells, XPO1 functions to transport critically important proteins out of the nucleus, but overexpression in cancer cells mediates transport of tumor suppressors such as p53, p73, FOXO, pRB, BRCA1, and PP2A (Figure 8). XPO1 is critical to this process as it appears to be the only nuclear exporter for most of these tumor suppressor proteins. In addition, XPO1 also appears to be involved in the control of several cellular processes by controlling the localization of cyclin B and MAP kinase. Selinexor binds to the Cys-528 residue in the cargo binding portion of XPO1, successfully preventing transport of these proteins from the nucleus to the cytoplasm; and thereby restoring normal cargo function. Reducing the efflux of these tumor suppressor proteins from the nucleus can have a deleterious impact on the function of cancer cells, enabling tumor cell progression to cellular senescence and apoptosis.

FIGURE 7. CRM1/XPO1 Mediates Nuclear to Cytoplasmic Cargo Transport



Source: Turner JG et al., Biochemical Pharmacology, 2012

FIGURE 8. Tumor Suppressor Proteins and Drug Targets that Undergo CRM1/XPO1 Mediated Trafficking

Protein	Functional significance	Export receptor	Modification required for nuclear export	Cancer type where protein is exported to the cytoplasm
Retinoblastoma	Tumor suppressor	CRM1	Phosphorylation by cyclin-dependent kinases	Retinoblastoma
APC	Tumor suppressor	CRM1	Single mutation causing frame-shift or premature termination	Colorectal cancer
p53	Tumor suppressor	CRM1	Ubiquitinylation by MDM2 E3 ubiquitin ligase	Colorectal cancer; breast cancer
BRCA1	Tumor suppressor	CRM1	BARD1 protein masks NES of BRCA1	Breast cancer
$p21^{CIP1}$	Cell cycle inhibitor	CRM1	HER2/neu mutation and phosphorylation by Akt; BCR-ABL translocation and phosphorylation by Akt; phosphorylation by PKC	Ovarian and breast cancer; chronic myeloid leukemia
Topoisomerase I	DNA topology, drug target	CRM1	Unknown	Anaplastic astrocytoma; neuroblastoma
Topoisomerase IIα	DNA topology, drug target	CRM1	Phosphorylation by casein kinase 2	Multiple myeloma
$p27^{KIP1}$	Cell cycle inhibitor	CRM1	Phosphorylation by human kinase-interacting stathmin (hKIS)	Breast cancer; acute myelogenous leukemia
FOXO	Tumor suppressor	CRM1	Phosphorylation by Akt kinase	Breast, prostate, and thyroid cancer; glioblastoma; melanoma
InI1/hSNF5	Tumor suppressor	CRM1	Mutation of conserved hydrophobic residues within the NES	Malignant rhabdoid tumors
BCR-ABL	Oncogene, tyrosine kinase	CRM1	Unknown	CML
Galectin-3	Regulator of cell proliferation and apoptosis	CRM1	Phosphorylation, casein kinase I	Thyroid, prostate, breast cancer
Bok	Pro-apoptotic factor	CRM1	Unknown	Breast cancer, HeLa cells
N-WASP/FAK	Regulator of actin cytoskeleton	CRM1	Phosphorylation by FAK (focal adhesion kinase), promoted by 17β-estradiol stimulation	Neural Wiskott-Aldrich syndrome, breast cancer, ovarian cancer
Nucleophosmin	Tumor suppressor	CRM1	Mutation of 288 and 290 tryptophan residues (AML), NF-kB/RelA masking (breast cancer)	Acute myeloid leukemia, breast cancer
Hsp90	Molecular chaperone	CRM1	Unknown	Breast cancer
Estradiol receptor	Blocks S-phase entry, cell-cycle	CRM1	PI3-kinase	Breast cancer
Tob	Cell-cycle inhibitor	CRM1	Unknown	Breast cancer
RASSF2	Tumor suppressor	CRM1	MAPK/ERK-2 phosphorylation	Thyroid cancer, nasopharyngeal carcinoma
Merlin	Tumor suppressor	CRM1	Unknown	Neurofibromatosis

Source: Turner JG et al., Biochemical Pharmacology, 2012

Selinexor Pre-clinical Proof of Concept

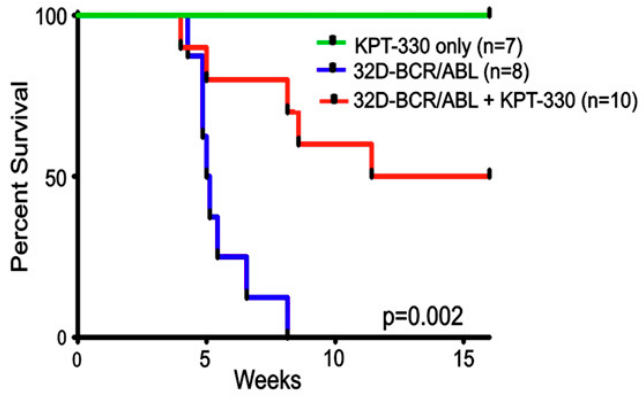
Selinexor's impact on numerous pathways critical to tumor biology highlights its potential utility in many hematological malignancies. Overexpression of XPO1 has been correlated with short survival in patients with acute myeloid leukemia (AML) (Kojima K, et al., *Blood*, 2013), chronic lymphoblastic leukemia (CLL) (Lapalombella, R, et al., *Blood*, 2012), chronic myelogenous leukemia (CML) (Neviani P, et al., *Cancer Cell*, 2005), and multiple myeloma (MM). To elucidate the mechanisms behind these clinical observations, significant pre-clinical research has been completed. This work provides meaningful support for progression to clinical studies of Selinexor in non-solid tumors.

Karyopharm scientists reported that in a panel of 14 human T-cell acute lymphoblastic leukemia (T-ALL) cell lines (Etchin J et al., *Br Jour Haem*, 2013), selinexor induced rapid apoptosis at low nanomolar concentrations. In addition, animal models demonstrated striking in vivo activity against T-ALL and AML cells, with little toxicity to normal murine hematopoietic cells. Selinexor has also been shown to restore normal regulation to malfunctioning pathways in CLL, including in genomically high-risk CLL cells that are typically unresponsive to traditional therapies. More importantly, selinexor has been shown to slow disease progression, and improves overall survival in an Eμ-TCL1-SCID mouse model of CLL with minimal weight loss or other toxicities (Figure 9). In leukemia cells that are Philadelphia positive (Ph^+), XPO1 is overexpressed, and treatment with selinexor decreases survival of Ph^+ leukemia, but not normal $CD34^+$ progenitors. In these cells, subversion of BCR-ABL1 transport restores activity of the protein phosphatase 2A (PP2A) tumor suppressor, allowing for the destruction of CML-BC and Ph^+ ALL blast cells (Figure 10).

Selinexor has also been shown to block c-myc, Mcl-1, and nuclear factor KB (NF-KB) activity that lead to disease progression and bone resorption in MM. Selinexor blocked RANKL-induced NF-Kb p65 activity in CD14+ osteoclast pre-cursor cells. As a result, selinexor completely blocked MM1S tumor cell growth in vitro (Figure 11) and in a murine xenograft model. CT imaging of vehicle-treated mice showed marked osteolysis (bone destruction) and reduction in bone mineral density. This resulted in reduced tumor size measured by bioluminescence in treated mice, and improved morbidity (Tai Y et al., *Leukemia,* 2013). Selinexor reduced MM cell viability in the nanomolar range when given as a single agent or in combination with doxorubicin, bortezomib or carfilzomib (Turner J, et al., *J Cancer*, 2013). Selinexor was also shown to sensitize MM cell lines and patient myeloma cells to these same drugs, but did not affect peripheral blood mononuclear or non-myeloma bone marrow mononuclear cells (Figure 12).

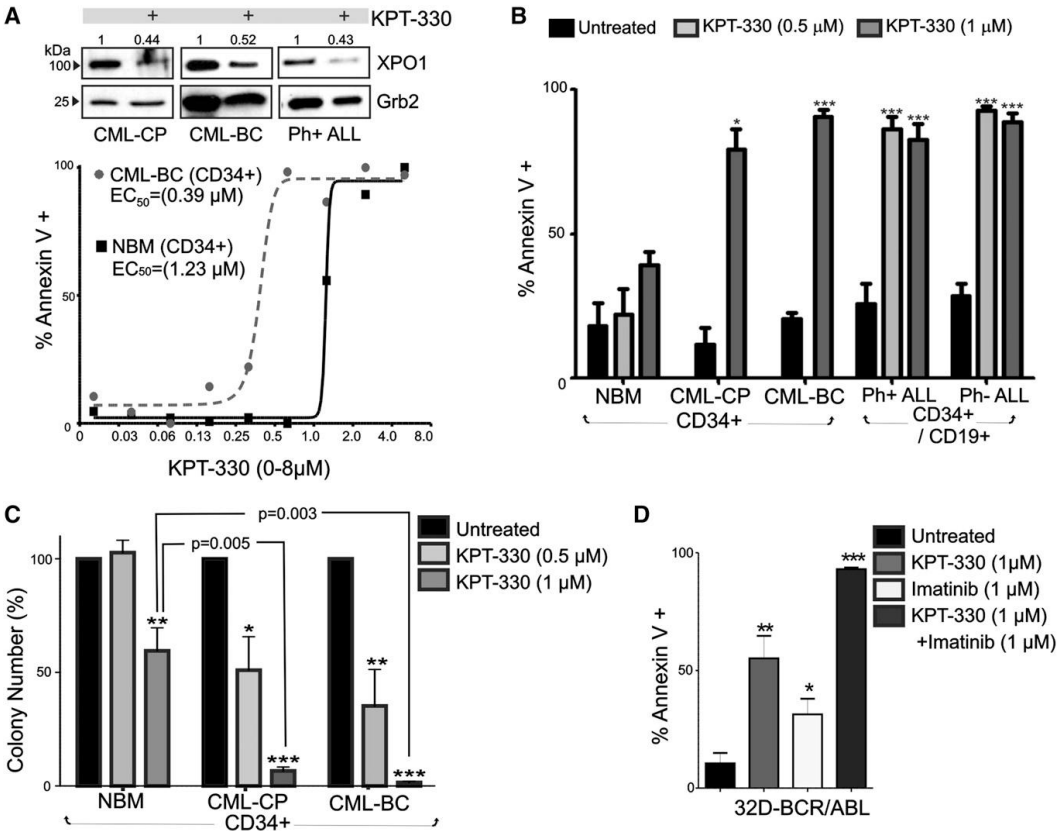
Taken together, these results show that selinexor represents a promising first-in-class drug with a novel mechanism of action and wide therapeutic index. The pre-clinical data for drugs in the SINE class will continue to support clinical trials for targeted therapy of AML, CLL, T-ALL, and MM. In addition, there are many potential synergies with existing drugs that will be explored for combination therapies in the not too distant future.

FIGURE 9. Selinexor (KPT-330) Prolongs Survival of 32D BCR/ABL Leukemic Mice



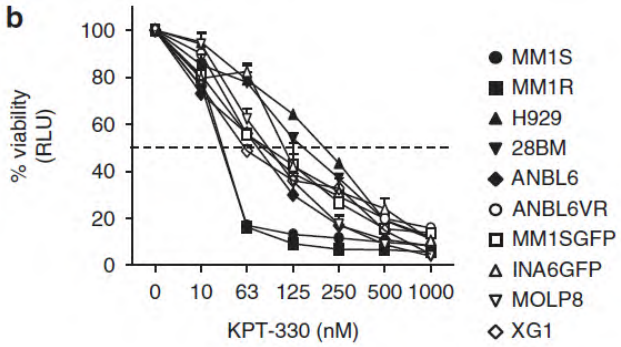
Source: Walker C, et al., doi:10.1182/blood-2013-04-495374

FIGURE 10. KPT-330 Decreased Survival and Clonogenic Potential in CML-BC and Ph$^+$ B-ALL Cells



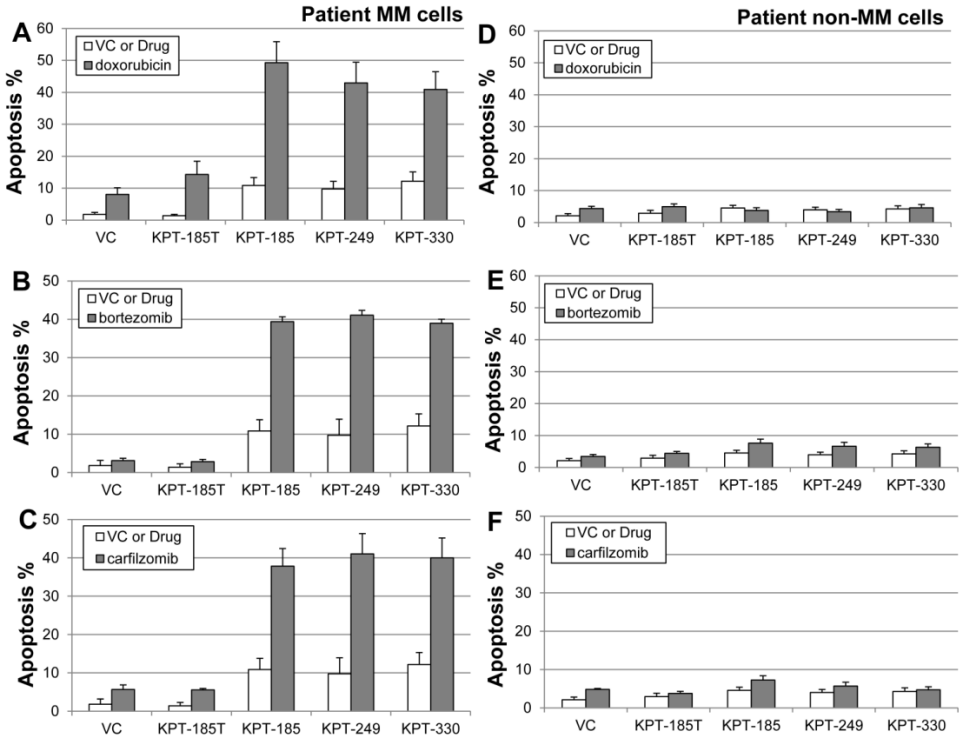
Source: Tai Y, et al. Nature doi:10.1038/leu.2013.115

FIGURE 11. Therapy Resistant Multiple Myeloma Cell Lines are Sensitive to Selinexor (KPT-330)



Source: Tai Y, et al. Nature doi:10.1038/leu.2013.115

FIGURE 12. KPT-330 Sensitizes Patient MM Cells to Doxorubicin, Bortezomib, and Carfilzomib



Source: Turner J et al., J of Cancer 2013

Selinexor Shows Promising Clinical Activity in Hematologic Malignancy

Investors being introduced to the Karyopharm story at this stage have the benefit of appreciable safety and preliminary clinical data in various hematologic and solid tumor malignancies. In June 2012, a Phase I dose escalation study of selinexor in various hematologic malignancies was initiated, and is being led by principal investigator John Byrd of Ohio State University. The trial was designed as a three-arm, multiple ascending dose finding study, evaluating selinexor administered orally two or three times per week on a 28-day cycle in 49 patients with B-cell malignancy (including multiple myeloma (MM), CLL, NHL and Waldenstrom's macroglobulinemia (WM); Arm 1), 34 patients with relapsed/refractory acute myeloid leukemia (Arm 2), and a recently initiated third arm in patients with T-cell lymphoma (Arm 3).

Data from 39 evaluable patients in Arm 1 were disclosed in September, showing clinical activity in patients with CLL, diffuse large B-cell lymphoma (DLBCL), WM, and MM (Figure 13), treated over a dose range of three to 45mg/m^2. Most of these patients were very heavily pre-treated, many progressing on their existing therapy when they entered the trial. Thus far, encouraging activity has been seen in patients with refractory CLL (n=5), where selinexor has achieved lymph node responses in three patients (60%) and stable disease in another two (40%). Of note, a 60% nodal response was observed in a patient whose disease had undergone Richter's transformation to DLBCL following prior chemotherapy and treatment with Imbruvica (Ibrutinib, PCYC, MO, $163 PT), and achieved within one

cycle of selinexor treatment. Similarly encouraging activity has been seen in patients with DLBCL (n=5), where one partial response (20%) and two (40%) cases of stable disease have been achieved, with a median duration of at least 2.6 months on therapy (as of July 2013) (Figure 14). A fixed-dose expansion cohort evaluation of 35mg/m^2 of selinexor in ~15 DLBCL patients was initiated in June, and should provide further clarity around the drug's efficacy in 1H14, or potentially at the upcoming ASH meeting in December.

Best response among patients with multiple myeloma (n=17) included one (6%) partial response, four (24%) minor responses (defined as 25-49% reduction in serum M protein without further increase in number or size of lytic bone lesions) and seven cases (41%) of stable disease (Figure 13 and 15). Several of these patients, including the patient with a partial response, had been treated with multiple prior therapies, including both proteasome inhibitor (Velcade) and immumodulatory agents (Revlimid and Pomalyst (CELG, MO, $175 PT)), suggesting selinexor's single-agent activity is potentially understated in the refractory setting. A fixed-dose expansion cohort in up to 10 patients with MM was also initiated in June, again offering the opportunity to better define the drug's single-agent activity in the indication.

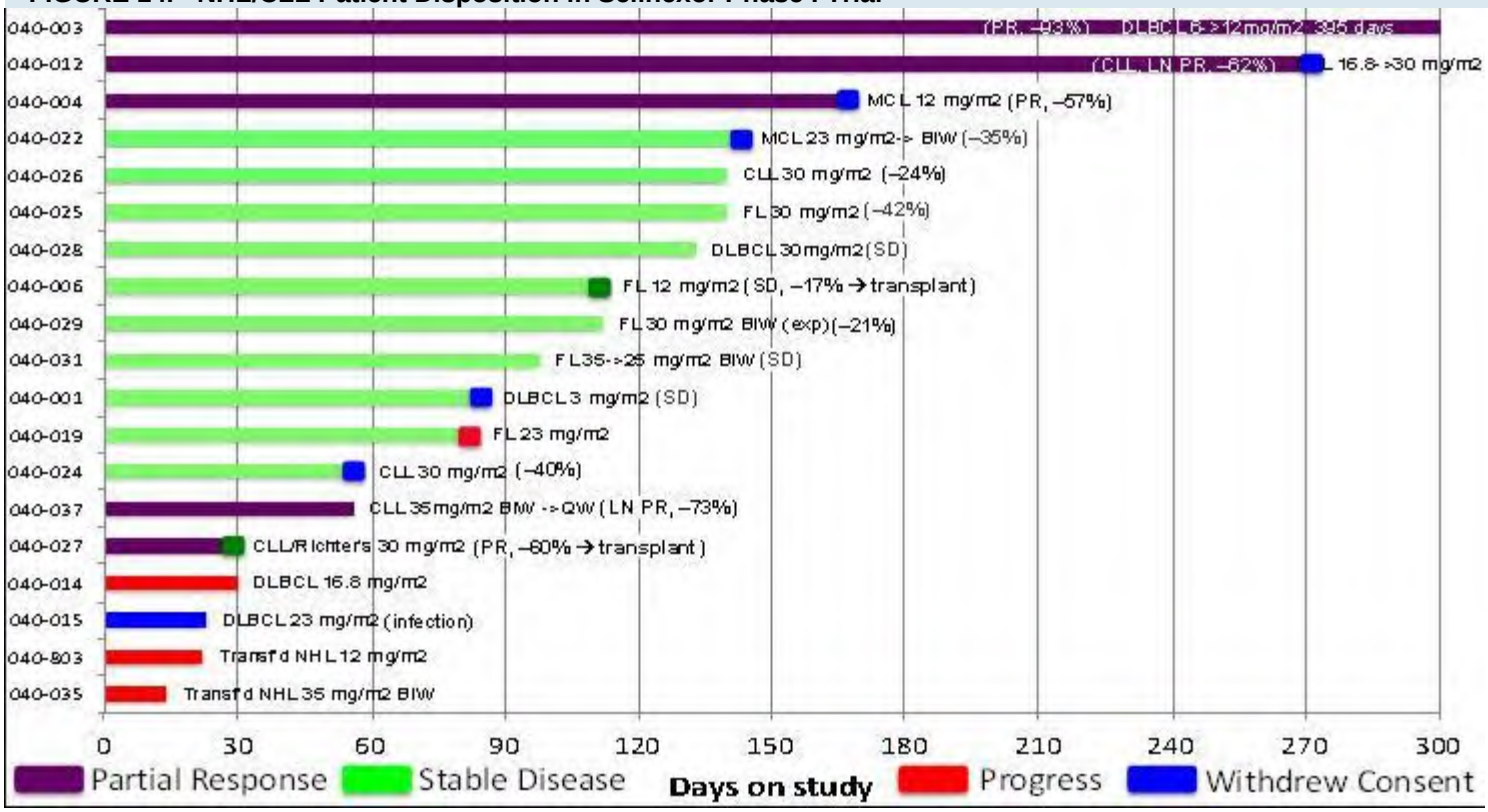
FIGURE 13. Phase I Selinexor Responses in B-Cell Malignancies

Phase I Selinexor Responses in B-Cell Malignancies					
Indication	Patients (n)	Best Response			
		PR (%)	MR (%)	SD (%)	PD (%)
MM	17	1 (6)	4 (24)	7 (41)	4 (24)
WM	2		2 (100)		
CLL	5	3* (60)		2 (40)	
NHL					
DLBLC	5	1 (20)		2 (40)	2 (40)
MCL	3	1 (33)		1 (33)	
FL	5			5 (100)	
Transformed	2				2 (100)
Total	**39**	**6 (15)**	**6 (15)**	**17 (44)**	**5 (21)**

*PR: partial reponse, * refer to nodal response only*
MR: minor response
SD: stable disease
PD: progressive disease
** refers to nodal response only*

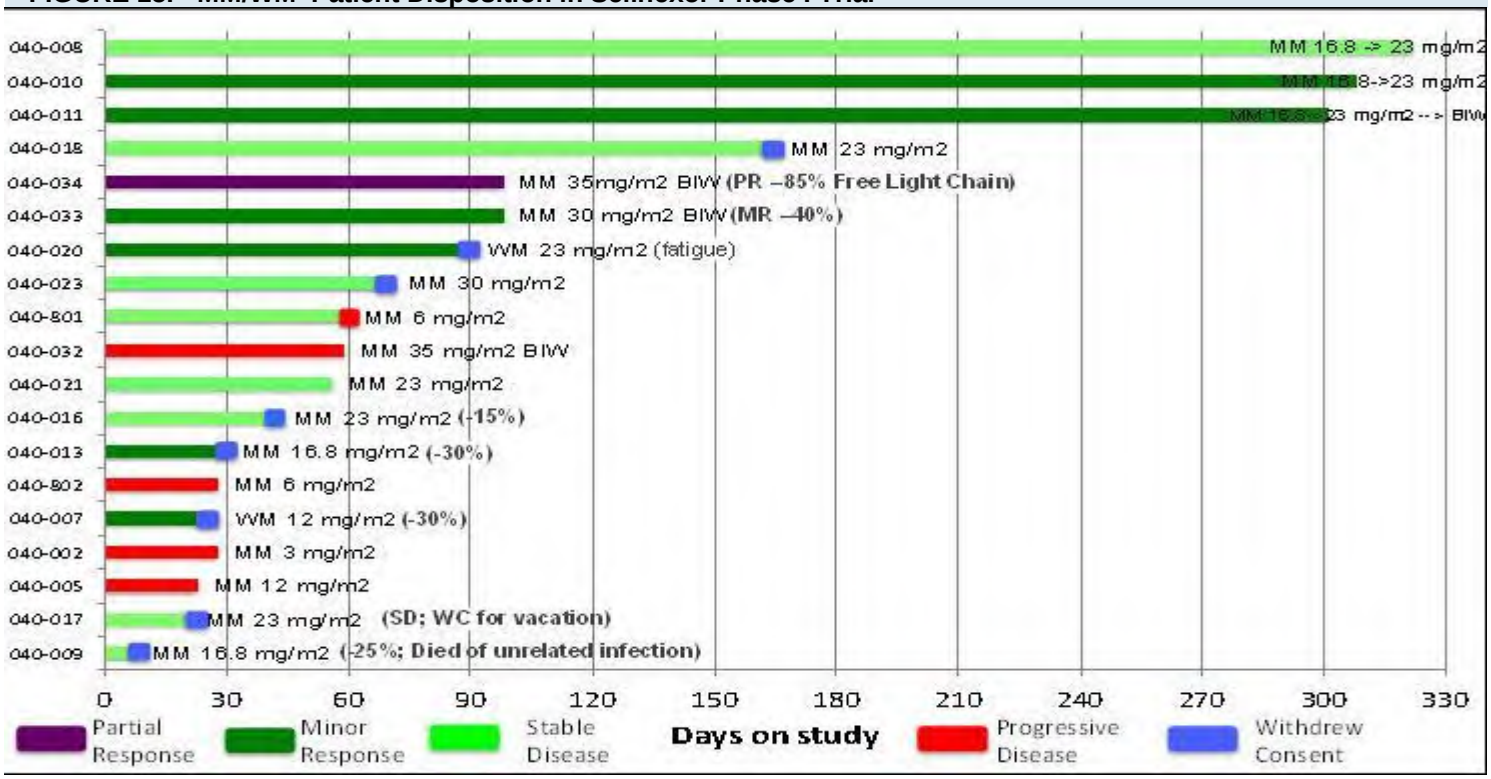
Source: Karyopharm Company reports

FIGURE 14. NHL/CLL Patient Disposition in Selinexor Phase I Trial



Source: Karyopharm Company reports

FIGURE 15. MM/WM Patient Disposition in Selinexor Phase I Trial



Source: Karyopharm Company reports

A second arm evaluating selinexor in relapsed/refractory AML was initiated in January 2013 and has thus far yielded complete remissions (with or without complete blood count recovery) in three (9%) patients, and disease stabilization in another twelve (38%) patients (Figure 16 and 17)), with an overall median duration of therapy of at least 1.4 months (as of July 26, 2013). Putting these results in the broader context, data thus far compare favorably with existing and next-generation HMA therapies (decitabine/azacitidine and SGI-110 (formerly ASTX, now Otsuka (JP-4578, NC)), respectively) and other nucleoside analogs (Sapacitabine, CYCC, MO, $9 PT) for a similarly refractory patient population.

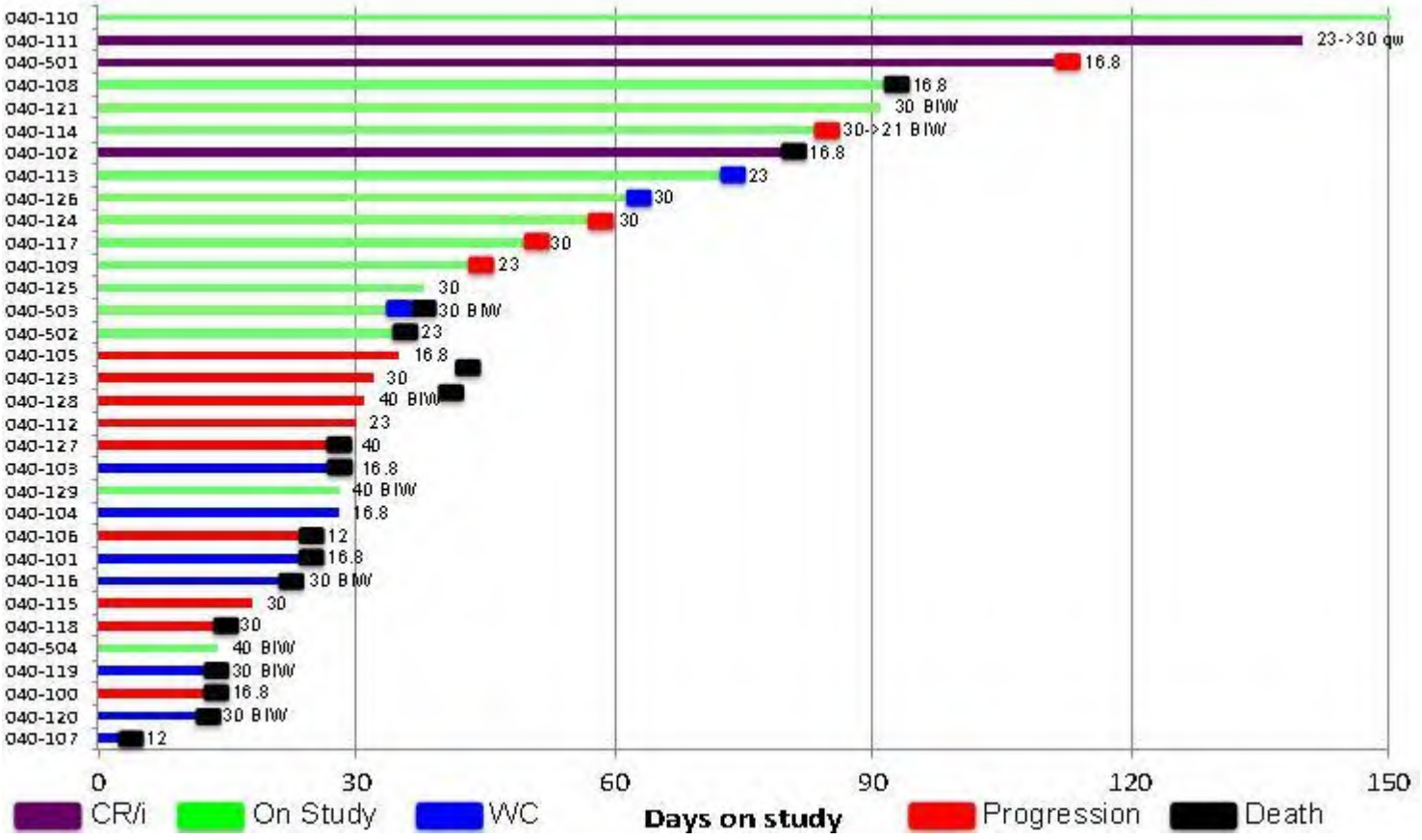
FIGURE 16. Phase I Selinexor Responses in Acute Myeloid Leukemia

Phase I Selinexor Responses in AML				
Evaluable/ Treated	Best Response			
	CR (%)	CRi (%)	SD (%)	PD (%)
32/34	2 (6)	1 (3)	12 (38)	11 (34)

CR: complete remission
CRi: CR with incomplete neutrophil or platelet count recovery
SD: stable disease
PD: progressive disease

Source: Karyopharm Company reports

FIGURE 17. AML Patient Disposition in Selinexor Phase I Trial



Source: Karyopharm Company reports

With respect to selinexor's safety profile, the most common side effects observed to date have been gastrointestinal in nature. Data from the 38 evaluable patients in Arm 1, as of September 20, show the most frequent side effects to be Grade 3 nausea (79%), anorexia (63%), vomiting (39%), and diarrhea (39%). Fatigue was reported in 53% of patients, including one Grade 3 event. Hematologic toxicities comprise the next most prominent category of side effects, including Grade 3/4 thrombocytopenia (31%) and neutropenia (29%). These events have largely been attributed to bone marrow suppression as a result of the underlying disease and the impact of prior therapy.

Similarly in the second arm of AML patients, low-grade gastrointestinal toxicities and fatigue comprise the majority of adverse events (nausea: 60%; anorexia: 57%; vomiting: 40%; weight loss: 23%; and fatigue: 53%, including 7% Grade 3). In response to these data, clinical trial protocols have been amended to require prophylaxis with supportive care to maintain caloric and fluid intake as well as anti-emetic medication prior to initiation of therapy.

Crossover Potential in Solid Tumors

In addition to hematologic indications, selinexor is under ongoing evaluation in the treatment of various refractory solid tumor malignancies. Data from a multiple-ascending Phase I study of selinexor disclosed in September have, thus far, shown largely stable disease as the best response (Figure 18), although partial response has been in patients with colorectal cancer and melanoma.

The adverse event profile in solid tumors has been rather similar to that observed in the heme malignancy studies with respect to high rates of low-grade GI toxicities and fatigue. By contrast, anemia has been the predominant hematologic adverse event rather than neutropenia or thrombocytopenia (Figure 19).

While present data would suggest limited potential for use as single agent, a more concrete picture is expected to mature from an ongoing fixed-dose expansion cohort, evaluating 35mg/m^2 across 30 patients with a mix of CRC, prostate, ovarian, head and neck, lung, and cervical squamous carcinomas.

FIGURE 18. Selinexor Phase I Solid Tumor Efficacy

Phase I Selinexor Responses in Solid Tumors				
Indication	Patients (n)	Best Response		
		PR (%)	SD (%)	PD (%)
Colorectal cancer	29	1 (3)	10 (34)	16 (55)
Head & Neck	9		4 (44)	4 (44)
Lung	6		4 (67)	2 (33)
Ovarian	7		3 (43)	2 (29)
Cervical	2		2 (100)	
Endometrial Stromal Sarcoma	2		2 (100)	
Melanoma	2	1 (50)	1 (50)	
Pancreas	5		1 (20)	1 (20)
Prostate	4		3 (75)	
Other	10		3 (30)	6 (60)
GBM	1			1 (100)
Total	**77**	**2 (3)**	**33 (43)**	**32 (42)**

Source: Karyopharm Company reports

FIGURE 19. Selinexor Phase I Solid Tumor Safety

Phase I Solid Tumor Adverse Events (n=68)		
	All Grade (%)	Grade 3/4 (%)
GI		
Nausea	81	1
Anorexia	74	
Vomiting	60	1
Diarrhea	31	
Dysgeusia	44	
Weight loss	40	1
Fatigue	79	15
Hematologic		
Anemia	29	9
Thrombocytopenia		
Neutropenia		
Withdrawl from study	7	

Source: Karyopharm Company reports

Pivotal Trial Development

Based on the clinical data to date with selinexor and the maturing competitive landscape, Karyopharm has identified newly diagnosed elderly AML and relapsed/refractory DLBCL as leading indications in its monotherapy registration strategy. Thus far, the company has articulated plans to initiate registration-directed studies in 1H14 beginning in either of these indications, although specific guidance regarding trial design has not yet been given. We anticipate that a registration-directed Phase II/III trial in front-line elderly AML would involve patient randomization against an active comparator of best supportive care of either low-dose cytarabine or HMA therapy and to enroll up to 140 patients in order to yield a statistically robust outcome using the primary endpoint of overall survival. Similarly for DLBCL, we anticipate that a potential pivotal study would adopt a randomized design against best supportive care in the post-transplant setting in patients who have had at least two prior lines of chemotherapy, and use a primary endpoint of overall survival.

Karyopharm has also articulated a goal of pursuing selinexor development in multiple myeloma. While the data at hand show promise, it is more likely that selinexor's future in this indication is that of a combination partner to proteasome or immunomodulatory agents. In that light, we would anticipate further Phase I or Ib evaluation in combination with Kyprolis or Pomalyst ahead of the initiation of registration directed trials in this indication. Our presumption is that any trials in the myeloma space will be facilitated by Dr. Kauffman's outstanding track record in myeloma drug development.

SELINEXOR COMMERCIAL POTENTIAL

Our Karyopharm revenue forecasts focus on selinexor's use in hematologic malignancy indications, where current clinical data and the competitive landscape would suggest the product candidate has its greatest chance of regulatory and commercial success. These include front-line elderly AML, relapsed/refractory diffuse large B-cell lymphoma, and relapsed/refractory multiple myeloma. As described in further detail below (Figures 20 to 23), our model predicts combined selinexor sales achieving $1 billion by 2021 in the U.S., growing to $1.7 billion by 2025, underscoring the drug's blockbuster potential.

Commercial projections in AML

Approximately 15,000 new cases of AML are diagnosed in the U.S. each year, according to SEER estimates, culminating in over 10,000 deaths. As highlighted above, whereas younger and fitter patients might be treated with 7+3 induction chemotherapy (seven consecutive days of cytarabine IV infusion followed by three consecutive days of anthracycline by IV push per 28-day cycle), patients over the age of 70 with greater comorbidity, typically receive low-intensity treatment with low-dose cytarabine or hypomethylating agents (HMA), such as Dacogen (Eisai/JNJ) and Vidaza (CELG).

This latter population of elderly front-line AML is where we believe selinexor can find a home with the broader treatment paradigm. Given a median age of onset of 67, it is estimated that ~45% of new diagnoses are patients 70 years of age and older. Our model assumes moderately increasing market penetration within this patient population plateauing at 60%, based largely on the evidence of its activity to date in a heavily pre-treated, relapsed/refractory patient population. As selinexor enjoys a favorable safety profile, well-distinguished from that of HMA therapy, it is likely these agents will ultimately be used in combination, and may prove our market uptake assumptions to be conservative.

Our projected duration of therapy (incrementally increasing from 5.7 months) is based on what we estimate as the duration of PFS accompanying a meaningful OS benefit relative to supportive care, low-dose cytarabine. In the U.S., our model forecasts over ~$300MM in sales by 2023. We assume similar demographic and market uptake dynamics for Europe and Japan beginning in 2017 and 2019, respectively, however, using a 20% discount to U.S. pricing in Europe, in order to arrive at $350MM in ex-U.S. sales. We further assume that ex-U.S. sales would be led by a strategic commercial partner delivering a straight-line 15% royalty on net sales to Karyopharm. This may also prove to be conservative as the company has hinted at the possibility of commercializing selinexor on its own in Europe.

Commercial projections in DLBCL

Non-Hodgkin's lymphoma (NHL) is the fifth most common lymphatic disease, diagnosed in nearly 70,000 cases in the United States in 2013, resulting in over 19,000 deaths. NHL can be roughly subcategorized into two groups, distinguished by differences in the rapidity of progression: 1) indolent disease, with a median survival between seven to ten years, and 2) aggressive disease, with an overall five-year survival rate of 50% (median of 2.5 years). Diffuse large B-cell lymphomas (DLBCL) comprise a substantial fraction of the aggressive disease, accounting for approximately 30% of those diagnosed with NHL annually. Although the data vary, they suggest a majority (55-80%) of patients enter remission with standard front-line anthracyclin- and Rituxan-based immunochemotherapy (R-CHOP) within one to two years. With the remainder progressing from first-line therapy, we model a second-line prevalence population of ~22,000 patients. Similarly, a minority of these patients are anticipated to progress from various second-line options, contributing to a third-line prevalence population of ~5,500 patients.

Our model projects selinexor use beginning in third-line DLBCL in 2017 in the U.S., before migrating to second-line therapy in subsequent years (with correspondingly longer-treatment periods). In both lines of therapy, we model moderately increasing market penetration, plateauing at 25%, to arrive at a revenue estimate of ~$800MM in 2025. We assume a similar demographic breakdown for Europe and Japan, beginning with baseline NHL incidence rates of nearly 94,000 and 13,000 patients, respectively. We also assume a similar market uptake dynamic to the U.S., beginning in 2018 for Europe and in 2020 in Japan. Our ex-U.S. sales forecasts reach ~$700MM in Europe and ~$155MM in Japan in 2025, culminating in $128MM royalty revenue to Karyopharm.

Commercial Projections in Multiple Myeloma

According to 2013 SEER estimates, the multiple myeloma prevalence population in the U.S. is approximately 77,600 patients and continues to grow with the advent and introduction of new therapies capable of extending survival rates. Segmentation of the overall prevalence population by line of therapy is difficult to pinpoint; however, our research suggests a roughly even distribution across the newly diagnosed, first relapsed/refractory (second-line), and multiple relapsed/refractory (third-line and above) patient populations. Our model assumes initial use as a later-line therapy beginning 2017 with moderately increasing market penetration to 20% by 2022, followed by migrating use to second-line, likely in combination with approved proteasome inhibitor and immunomodulatory therapies, beginning in 2019. In all, our model forecasts sales of $634MM in the U.S. from multiple myeloma by 2025. Again, we assume a similar demographic breakdown and market uptake dynamics for Europe and Japan, starting with prevalence populations of 76,700 and 12,400 patients, respectively. We forecast $308MM sales in Europe and ~$100MM in Japan in 2025, delivering $60MM in royalty revenue to Karyopharm.

FIGURE 20. Summary of Selinexor Revenue Forecast by Indication and Region

Selinexor Revenue Summary	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
WW Sales	**$ 18**	**$ 117**	**$ 343**	**$ 755**	**$ 1,318**	**$ 2,003**	**$ 2,583**	**$ 2,991**	**$ 3,212**	**$ 3,364**
US	18	86	262	516	849	1,199	1,447	1,617	1,689	1,760
Ex-US Sales	-	30	81	239	469	804	1,136	1,374	1,523	1,604
Effective royalty rate	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
Royalty Revenue to KPTI	**$ -**	**$ 5**	**$ 12**	**$ 36**	**$ 70**	**$ 121**	**$ 170**	**$ 206**	**$ 228**	**$ 241**
Breakdown by Geography and Indication										
US	**$ 18**	**$ 86**	**$ 262**	**$ 516**	**$ 849**	**$ 1,199**	**$ 1,447**	**$ 1,617**	**$ 1,689**	**$ 1,760**
AML	18	58	99	150	213	254	288	299	311	323
MM	-	22	95	180	279	417	530	580	607	634
DLBCL	-	6	69	186	356	528	630	738	771	802
EU	**$ -**	**$ 30**	**$ 81**	**$ 226**	**$ 435**	**$ 713**	**$ 983**	**$ 1,146**	**$ 1,235**	**$ 1,251**
AML	-	30	62	99	139	192	221	242	243	244
MM	-	-	13	53	100	166	239	299	303	308
DLBCL	-	-	6	74	196	355	523	606	689	699
JPN	**$ -**	**$ -**	**$ -**	**$ 13**	**$ 34**	**$ 92**	**$ 152**	**$ 227**	**$ 288**	**$ 353**
AML	-	-	-	13	25	44	61	77	91	106
MM	-	-	-	-	8	32	51	72	83	93
DLBCL	-	-	-	-	1	15	40	78	114	155

Source: JMP Securities LLC and Company reports

FIGURE 21. Selinexor Revenue Model in AML

US													
Selinexor for Elderly AML ($MM)	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Elderly AML													
AML indicence, US	14,676	14,896	15,120	15,346	15,577	15,810	16,047	16,288	16,532	16,780	17,032	17,288	17,547
%Growth		*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*
% pts > 70 yrs of age	*45%*	*44.8%*	*44.5%*	*44.3%*	*44.0%*	*43.8%*	*43.5%*	*43.3%*	*43.0%*	*42.8%*	*42.5%*	*42.3%*	*42.0%*
Addressable ederly AML patient population	6,604	6,666	6,728	6,791	6,854	6,917	6,981	7,045	7,109	7,174	7,239	7,304	7,370
Market penetration				*5%*	*15%*	*24%*	*35%*	*48%*	*55%*	*60%*	*60%*	*60%*	*60%*
Elderly AML patients on Selinexor	-	-	-	340	1,028	1,660	2,443	3,381	3,910	4,304	4,343	4,382	4,422
Duration of therapy (cycles)				5.7	5.8	5.9	5.9	5.9	5.9	5.9	5.9	5.9	5.9
Total patient cycles on therapy	-	-	-	1,935	5,963	9,794	14,415	19,950	23,068	25,395	25,625	25,856	26,089
Cost of therapy (per cycle)				$ 9,500	$ 9,785	$ 10,079	$ 10,381	$ 10,692	$ 11,013	$ 11,343	$ 11,684	$ 12,034	$ 12,395
% price increase					*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
US sales of Selinexor				**$ 18.4**	**$ 58.3**	**$ 98.7**	**$ 149.6**	**$ 213.3**	**$ 254.1**	**$ 288.1**	**$ 299.4**	**$ 311.2**	**$ 323.4**
% Growth					*217%*	*69%*	*52%*	*43%*	*19%*	*13%*	*4%*	*4%*	*4%*

Source: JMP Securities LLC and Company reports

FIGURE 22. Selinexor Revenue Model in DLBCL

US													
Selinexor for DLBLC ($MM)	**2013E**	**2014E**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**
DLBCL													
NHL Incidence, US	67,694	68,371	69,055	69,745	70,443	71,147	71,859	72,577	73,303	74,036	74,776	75,524	76,279
% Growth		*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*
% DLBCL	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*	*29%*
Number of 1L DLBCL Patients	19,631	19,828	20,026	20,226	20,428	20,633	20,839	21,047	21,258	21,470	21,685	21,902	22,121
% treated with chemotherapy	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*
1L Treated DLBCL Patients	14,723	14,871	15,019	15,170	15,321	15,474	15,629	15,786	15,943	16,103	16,264	16,426	16,591
Second-Line (2L) DLBCL													
Five-Year Prevalence of DLBCL	73,617	74,353	75,097	75,848	76,606	77,372	78,146	78,928	79,717	80,514	81,319	82,132	82,954
% Second-Line	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Addresable 2L DLBCL Patients	22,085	22,306	22,529	22,754	22,982	23,212	23,444	23,678	23,915	24,154	24,396	24,640	24,886
Market Penetration						**3%**	**8%**	**14%**	**20%**	**22%**	**25%**	**25%**	**25%**
2L patients on Selinexor	-	-	-	-	-	696	1,876	3,315	4,783	5,314	6,099	6,160	6,222
Duration of Therapy (cycles)						7.0	7.5	8.0	8.5	9.0	9.0	9.0	9.0
2L cycles on therapy	-	-	-	-	-	4,874	14,066	26,520	40,656	47,825	54,890	55,439	55,994
Cost of therapy					$ 9,785	$ 10,079	$ 10,381	$ 10,692	$ 11,013	$ 11,343	$ 11,684	$ 12,034	$ 12,395
Price incresae						*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
2L Selinexor Sales, US ($MM)					**$ -**	**$ 49.1**	**$ 146.0**	**$ 283.6**	**$ 447.7**	**$ 542.5**	**$ 641.3**	**$ 667.2**	**$ 694.1**
Third-Line (3L) DLBCL													
% progressing from 2L	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*
Addresable 3L DLBCL Patients	5,521	5,577	5,632	5,689	5,745	5,803	5,861	5,920	5,979	6,039	6,099	6,160	6,222
Market Penetration					**3%**	**8%**	**15%**	**25%**	**25%**	**25%**	**25%**	**25%**	**25%**
3L patients on Selinexor					144	464	879	1,480	1,495	1,510	1,525	1,540	1,555
Duration of Therapy (cycles)					4.0	4.2	4.4	4.6	4.9	5.1	5.4	5.6	5.6
3L cycles on therapy					575	1,950	3,868	6,808	7,324	7,699	8,234	8,624	8,710
Cost of therapy					$ 9,785	$ 10,079	$ 10,381	$ 10,692	$ 11,013	$ 11,343	$ 11,684	$ 12,034	$ 12,395
Price incresae						*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
3L Selinexor Sales, US ($MM)					**$ 5.6**	**$ 19.7**	**$ 40.2**	**$ 72.8**	**$ 80.7**	**$ 87.3**	**$ 96.2**	**$ 103.8**	**$ 108.0**

Source: JMP Securities LLC and Company reports

FIGURE 23. Selinexor Revenue Model in MM

US													
Selinexor for Multiple Myeloma ($MM)	**2013E**	**2014E**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**
Multiple Myeloma													
MM Prevalence, US	77,617	78,781	79,963	81,162	82,380	83,616	84,870	86,143	87,435	88,746	90,078	91,429	92,800
% Growth		*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*
Second-Line (2L) MM													
Number of 2L MM Patients	25,614	25,998	26,388	26,784	27,185	27,593	28,007	28,427	28,854	29,286	29,726	30,172	30,624
% of total	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*
Proportion treated with Chemotherapy	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*
Addressable 2L MM population	17,930	18,198	18,471	18,749	19,030	19,315	19,605	19,899	20,197	20,500	20,808	21,120	21,437
Market Penetration							***2%***	***4%***	***7%***	***9%***	***10%***	***10%***	***10%***
2L patients on Selinexor	-	-	-	-	-	-	392	796	1,414	1,845	2,081	2,112	2,144
Duration of Therapy (cycles)							6.7	9.0	10.2	11.0	11.0	11.0	11.0
2L cycles on therapy							2,627	7,164	14,421	20,295	22,889	23,232	23,581
Cost per cycle therapy					$ 9,785	$ 10,079	$ 10,381	$ 10,692	$ 11,013	$ 11,343	$ 11,684	$ 12,034	$ 12,395
Price increase						*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
2L Selinexor Sales, US ($MM)					**$ -**	**$ -**	**$ 27.3**	**$ 76.6**	**$ 158.8**	**$ 230.2**	**$ 267.4**	**$ 279.6**	**$ 292.3**
Third-Line and Beyond (3L+) MM													
Number of 3L+ MM Patients	22,897	23,240	23,589	23,943	24,302	24,667	25,037	25,412	25,793	26,180	26,573	26,972	27,376
% of total	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Proportion treated with Chemotherapy	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*
Addressable 3L+ MM population	16,028	16,268	16,512	16,760	17,011	17,267	17,526	17,788	18,055	18,326	18,601	18,880	19,163
Market Penetration					***2%***	***8%***	***12%***	***15%***	***18%***	***20%***	***20%***	***20%***	***20%***
3L+ patients on Selinexor	-	-	-	-	340	1,381	2,103	2,668	3,250	3,665	3,720	3,776	3,833
Duration of Therapy (cycles)					6.7	6.8	7.0	7.1	7.2	7.2	7.2	7.2	7.2
3L+ cycles on therapy					2,280	9,393	14,722	18,945	23,400	26,390	26,786	27,187	27,595
Cost per cycle therapy					$ 9,785	$ 10,079	$ 10,381	$ 10,692	$ 11,013	$ 11,343	$ 11,684	$ 12,034	$ 12,395
Price increase						*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
3L+ Selinexor Sales, US ($MM)					**$ 22.3**	**$ 94.7**	**$ 152.8**	**$ 202.6**	**$ 257.7**	**$ 299.4**	**$ 313.0**	**$ 327.2**	**$ 342.1**

Source: JMP Securities LLC and Company reports

COMPETITIVE LANDSCAPE

The competitive landscape for selinexor can be viewed from two perspectives: first, in relation other inhibitors of XPO1 or other nuclear transporters, and second, in relation to developing and commercially available oncology medicines.

Selinexor enjoys relatively little competition with respect to mechanism of action in that there appear to be only two competitor XPO1 inhibitor programs, both of which are pre-clinical and of unknown or discontinued status. CBS9106 is a novel, reversible XPO1 inhibitor in development at Japan-based CanBas Co. (private). Pre-clinical experiments published in 2011 show CBS9106 to be similarly active against tumor models both in vitro and in vivo, albeit with lower potency. By our checks, clinical evaluation of CBS9106 has not yet been pursued, however. CBS9106 was preceded by work at Kosan Biosciences (since acquired by Bristol-Myers (BMY, NC) and the development of KOS-2464 - a synthetic derivative of the antibiotic molecule leptomycin B (LMB). Like LMB and selinexor, KOS-2464 is an irreversible inhibitor of XPO1 binding to the active site cysteine residue Cys528. Pre-clinical studies showed KOS-2464 to have potent, in vivo antitumor activity across solid tumor and leukemic xenograft models, but with less of the off-target toxic effects seen with LMB, thus translating into greater tolerability in mice. As we previously mentioned, KOS-2464 has not been brought forward to the clinic and its development status remains unknown.

Within the broader AML treatment landscape, selinexor faces competition for approved hypomethylating agents decitabine (Dacogen, marketed by Eisai, NC) and azacitidine Vidaza as well as from next-generation HMA product candidates such as SGI-110 (ASTX, now Otsuka). Dacogen was approved for the treatment of elderly AML in the EU in September 2012, and while not formally approved in the U.S. outside of MDS, it is estimated that upwards of 15-20% of AML patients over the age of 70 are treated with decitabine. Vidaza is also in development for use as front-line elderly AML therapy, currently in a Phase III trial versus best supportive care. SGI-110, a pro-drug version of decitabine, is currently in Phase II assessment in both MDS and AML showing compelling signals in relapse/refractory patients with prior exposure to HMA therapy. Sunesis' (SNSS, NC) topoisomerase II inhibitor, vosaroxin, also presents some tangential competition in AML. Vosaroxin is presently being developed in the relapsed/refractory AML setting as a combination agent to lose-dose cytarabine (the VALOR Phase III trial); however, it is reasonable to foresee some front-line use in the elderly setting if ultimately approved. Given the favorable safety profile of selinexor, in addition to pre-clinical data suggesting the potential for enhanced antitumor activity through synergistic mechanisms of action, we believe that it is more likely the case that selinexor will mature into being a frequent combination agent with both classes of therapy rather than standing direct competition.

We view the competitive landscape in DLBCL and multiple myeloma much in the same way. Non-chemotherapy based treatment options in the transplant ineligible, relapsed/refractory DLBCL setting remain largely in development. Revlimid (CELG) is currently recommended for those patients with non-germinal center subtype disease, while Imbruvica (PCYC) has also shown activity and is expected to ultimately be used in same patient population. By contrast, selinexor development is not expected to be relegated to a particular histology. Its use may overlap with that of Revlimid and Imbruvica; however, we believe there to be a strong potential that these agents are used in combination. The same can be said for the oral immunomodulatory drug Pomalyst (CELG) and the proteasome inhibitors Velcade (Takeda) and Kyprolis (AMGN, NC) in multiple myeloma.

SUMMARY AND CONCLUSION

As previously stated, we believe Karyopharm has all the elements under one roof to enable enormous success in oncology drug discovery. The company has a dominant position in the biology of nuclear exportins, superb chemistry that allows the company to produce potent and selective inhibitors of XPO1/CRM1, and a committed management team with a proven track record of successful clinical development and commercial strategy. Investors have enjoyed significant gains in the shares of a number of companies in the oncology space when their lead programs show preliminary signs of efficacy in genetically targeted tumors. Among these we would include Pharmacyclics (PCYC, MO), Puma Biotechnology (PBYI, NC), Clovis Oncology (CLVS, NC) and Tesaro (TSRO, NC). Our excitement over KPTI is based on the fact that the company is developing a potentially broad-based cancer therapy with early signs of significant activity, and we believe it will continue to produce value-driving clinical and pre-clinical data over the next 12-24 months.

Should the KPTI story unfold in a similar manner as the other companies we mentioned, investors could enjoy significant return on investment, with added potential value accretion coming from the near-term launch of verdinexor for the treatment of canine lymphoma (presently excluded from our valuation). Therefore, we are initiating coverage of KPTI with a Market Outperform rating and 12-month price target of $25.

FIGURE 24. Karyopharm Therapeutics Income Statement

Income Statement ($MM)	2011A	2012A	1Q-2Q13A	3Q13E	4Q13E	2013E	1Q14E	2Q13E	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Product Sales and Royalties:																	
Selinexor																	
US Sales												-	18.4	86.3	262.2	515.9	848.8
ROW Royalties												-	-	4.6	12.2	35.8	70.4
Total Product Sales and Royalties	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	18.4	90.8	274.3	551.7	919.2
Collaboration Revenue	0.2	0.6	0.4														
Total Revenue	0.2	0.6	0.4	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	18.4	90.8	274.3	551.7	919.2
Cost of Goods Sold													1.8	7.8	21.0	41.3	67.9
Gross Profit	0.2	0.6	0.4	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	16.5	83.1	253.4	510.4	851.3
Operating Expenses:																	
Research and Development	8.6	14.1	11.0	6.0	6.5	23.5	7.5	8.8	10.1	11.7	38.1	47.6	78.6	106.1	118.8	128.3	134.7
General and administrative	1.8	2.4	1.8	0.9	1.1	3.8	1.2	1.3	2.5	4.0	9.0	53.7	77.9	95.4	109.7	120.7	132.7
Total operating expenses	10.5	16.5	12.8	6.9	7.6	27.3	8.7	10.1	12.6	15.7	47.1	101.3	156.4	201.5	228.5	249.0	267.5
Operating income (loss)	(10.3)	(15.9)	(12.5)	(6.9)	(7.6)	(26.9)	(8.7)	(10.1)	(12.6)	(15.7)	(47.1)	(101.3)	(139.9)	(118.4)	24.8	261.5	583.8
Other income (expense):																	
Interest income	0.0	0.0	0.0			0.0											
Interest expense	0.0	0.0	0.0			0.0											
Total other income, net	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Change in fair value of preferred stock warrant liability	0.0	0.0	0.0														
Foreign currency transaction gain (loss)	0.0	0.0	0.0														
Pretax income (loss)	(10.3)	(15.9)	(12.5)	(6.9)	(7.6)	(26.9)	(8.7)	(10.1)	(12.6)	(15.7)	(47.1)	(101.3)	(139.9)	(118.4)	24.8	261.5	583.8
Income tax benefit (provision)											0.0	0.0	0.0	0.0	0.0	0.0	(87.6)
Tax Rate											*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*15%*
Comprehensive income (loss)	(10.3)	(15.9)	(12.5)	(6.9)	(7.6)	(26.9)	(8.7)	(10.1)	(12.6)	(15.7)	(47.1)	(101.3)	(139.9)	(118.4)	24.8	261.5	496.3
Accretion of redeemable convertible preferred stock	0.0	0.0	0.0														
Net income (loss) attributable to common stockholders	(10.3)	(15.9)	(12.5)	(6.9)	(7.6)	(26.9)	(8.7)	(10.1)	(12.6)	(15.7)	(47.1)	(101.3)	(139.9)	(118.4)	24.8	261.5	496.3
Basic EPS to common shareholders	$ (10.27)	$ (8.95)	$ (5.39)	$ (0.31)	$ (0.29)	$ (1.22)	$ (0.30)	$ (0.35)	$ (0.44)	$ (0.55)	$ (1.64)	$ (3.52)	$ (4.56)	$ (3.64)	$ 0.76	$ 7.99	$ 15.12
Diluted EPS to common shareholders	$ (10.27)	$ (8.95)	$ (5.39)	$ (0.31)	$ (0.29)	$ (1.22)	$ (0.30)	$ (0.35)	$ (0.44)	$ (0.55)	$ (1.64)	$ (3.52)	$ (4.56)	$ (3.64)	$ 0.74	$ 7.77	$ 14.70
Basic shares outstanding	1.0	1.8	2.3	21.9	25.9	22.2	28.7	28.8	28.8	28.8	28.8	28.8	30.6	32.5	32.6	32.7	32.8
Diluted shares outstanding	1.0	1.8	2.3	21.9	25.9	22.2	28.7	28.8	28.8	28.8	28.8	28.8	30.6	32.5	33.5	33.7	33.8
% change in diluted shares outstanding		*76.8%*		*0.2%*	*0.2%*						*29.8%*	*0.2%*	*6.3%*	*6.0%*	*3.2%*	*0.3%*	*0.3%*

Source: JMP Securities LLC, Company reports

APPENDIX A - MANAGEMENT TEAM AND BOARD OF DIRECTORS

Executive Management

Michael G. Kauffman, M.D., Ph.D., President, CEO, and CMO. Dr. Kauffman co-founded Karyopharm with Dr. Sharon Shacham in 2008 and has served as its President and Chief Executive Officer since January 2011, as Chief Medical Officer since December 2012, and as a director since 2008. Prior to joining Karyopharm, he was Chief Medical Officer of Onyx Pharmaceuticals Inc. (now Amgen, NC) from November 2009 to December 2010, which acquired Proteolix Inc. in November 2009 where he was Chief Medical Officer since November 2008, where he led the development of Kyprolis (carfilzomib), a novel proteasome inhibitor approved in refractory myeloma by the FDA in July 2012. Prior to joining Onyx, Dr. Kauffman was an operating partner at Bessemer Venture Partners from 2006 to 2008. Prior to that, he was President and Chief Executive Officer of Epix Pharmaceuticals, Inc., and President and Chief Executive Officer of Predix Pharmaceuticals, Inc. From March 2000 to September 2002, Dr. Kauffman was Vice President, Clinical at Millennium Pharmaceuticals, Inc., where he led the Velcade development program. Dr. Kauffman also currently serves on the board of directors for Verastem, Zalicus Inc., and Metamark Genetics Inc. (private). 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 Deaconness Medical Center and Massachusetts General Hospitals. He is board certified in internal medicine.

Sharon Shacham, Ph.D., Chief Scientific Officer and President, R&D. Dr. Shacham co-founded Karyopharm in 2008 and has served as its Chief Scientific Officer and President of Research and Development since December 2012, as its Chief Scientific Officer and Head of Research and Development from October 2010 to December 2012 and as its President and Chief Executive Officer from October 2010 to January 2011. Dr. Shacham has led the company's scientific progress since inception. Prior to joining Karyopharm, she was Senior Vice President of Drug Development at Epix Pharmaceuticals, Inc., from 2000 to April 2009, and Director, Algorithm and Software Development at Predix Pharmaceuticals Inc., which merged into Epix Pharmaceuticals in 2006. Dr. Shacham received her B.Sc. in Chemistry, Ph.D. and M.B.A. from Tel Aviv University.

Paul Brannelly, SVP, Finance and Administration. Mr. Brannelly joined Karyopharm in June 2013 as Senior Vice President, Finance and Administration and has served as its Secretary and Treasurer since July 2013. Prior to joining Karyopharm, Mr. Brannelly served most recently as Vice President of Finance at Verastem, Inc. From January 2010 to September 2011, Mr. Brannelly held the position of Chief Financial Officer at the Longwood Fund, where he set up the financial and operational infrastructure following the closing of its first fund. From November 2005 to September 2009, he served as Vice President, Finance at Sirtris Pharmaceuticals, Inc (now GSK). Prior to that, Mr. Brannelly held various positions of increasing responsibility at Zalicus Inc. from May 2005 to November 2005, most recently as VP Finance and Treasurer, and at Dyax Corporation from September 1999 to May 2002. Mr. Brannelly holds a Bachelor of Business Administration in Accounting from the University of Massachusetts.

Dilara McCauley Ph.D., VP, Product Leadership. Dilara McCauley, Ph.D., joined Karyopharm as Senior Director of Product Leadership. Before that she was the Director of Biology at Repligen Corporation, Epix and Predix Pharmaceuticals. She has authored more than 30 scientific publications and patents. She received her Ph.D. from the University of California, Santa Cruz.

Jamie Jamshidi, VP, Quality Assurance and Regulatory Affairs. Jamie Jamshidi has over 26 years of industry experience, including small molecules and large molecule biological, including 17 years of service at Amgen, Inc. where she supported the launches of Epogen® , Neupogen® and Sensipar® and established the departments of Contract Manufacturing and Small Molecule Quality Assurance at the company. In March 2007, Ms. Jamshidi founded Quality and Regulatory Management, Inc., a consulting firm providing expert technical services, solutions, and training to pharmaceutical and biopharmaceutical companies worldwide.

Robert Carlson Ph.D., VP, Preclinical Development. Robert Carlson, Ph.D. joined Karyopharm in September 2013 as Vice President, Preclinical Development, bringing with him over 20 years of drug discovery and development experience in a wide variety of therapeutic areas in both small and large companies. Just prior to Karyopharm, he was Vice President and Head of the Seattle site of JW Pharmaceuticals. From 2004 to 2012, he was Vice President and Head of Research in the Pharmaceutical Division of Myriad Genetics and the subsequent spinout Myrexis (private), which focused on cancer drug discovery and development. From 2001 to 2004, he was Director of Biology at Karo Bio, a biotech company specializing in nuclear hormone receptor drug discovery. Prior to that, he spent a decade working in Big Pharma for Bayer and Hoechst-Roussel (now Sanofi) on cancer, inflammation and neurodegeneration drug discovery. He earned a B.S. in Biochemistry from the University of Wisconsin-Madison, a Ph.D. in Biochemistry from Brandeis University and had postdoctoral training at the University of Michigan and Georgetown University.

Brian Austad Ph.D., Senior Director, Head of Pharmaceutical Sciences. Brian Austad, Ph.D., is a senior scientific leader in chemical and pharmaceutical development with 14+ years of pharmaceutical experience. He has extensive experience in natural product synthesis and natural product derivatives; complex chemistry; and optimizing API synthetic routes and manufacturing. Brian has been a Sr. Advisor in Chemical Development with Rondaxe Pharma (private) and was director of Process Chemistry at Infinity Pharmaceuticals where he established and built a highly effective process chemistry group responsible for the API development and manufacture of all Infinity clinical programs. He has previously worked at Eisai Research Institute as a scientist and project leader in process chemistry where he was a core contributor the development and manufacture of Halavan®. Brian received his B.S. degree in Chemistry from University of Wisconsin – Eau Claire and his Ph.D. in Synthetic Organic Chemistry from the University of Wisconsin – Madison.

John McCartney Ph.D., Senior Director, Product Leadership. John McCartney has joined Karyopharm as a Senior Director of Product Leadership to oversee KPT-330 clinical development. John has over 20 years of drug development and project management experience, working previously with GliaMed (private), EPIX Pharmaceuticals, Point Therapeutics (now Dara BioSciences), Cystic Fibrosis Foundation Therapeutics (non-profit) and Curis. John received his Ph.D. in Microbiology from Duke University and postdoctoral training at the Massachusetts Institute of Technology.

Source: Company website

Board of Directors

Michael G. Kauffman M.D., Ph.D.

Barry E. Greene. Mr. Greene has served as a member of Karyopharm's board of directors since January 2013. Mr. Greene has served as President and Chief Operating Officer of Alnylam Pharmaceuticals, Inc, since 2007, as its Chief Operating Officer since 2003, and from 2004 through 2005, as its Treasurer. Mr. Greene joined Alnylam in 2003, bringing over 15 years of experience in the healthcare industry and in consulting. Prior to Alnylam, he was General Manager of Oncology at Millennium Pharmaceuticals, Inc., where he led the company's global strategy and execution for its oncology business. Prior to Millennium, Mr. Greene served as Executive Vice President and Chief Business Officer for Mediconsult.com, a healthcare consulting company. Prior to Mediconsult.com, Mr. Greene's experiences included serving as Vice President of Marketing and Customer Services for AstraZeneca, and a partner of Andersen Consulting, a consulting company. Mr. Greene currently is a member of the boards of directors of public biopharmaceutical company Acorda Therapeutics, Inc. Mr. Greene received his B.S. in Industrial Engineering from the University of Pittsburgh and serves as a Senior Scholar at Duke University, Fuqua School of Business.

Deepa R. Pakianathan Ph.D. Dr. Pakianathan has served as a member of Karyopharm's board of directors since April 2013. Since 2001, Dr. Pakianathan has been a Managing Member at Delphi Ventures, a venture capital firm focused on medical device and biotechnology investments, and leads the firm's biotechnology investment activities. From 1998 to 2001, Dr. Pakianathan was a senior biotechnology banker at JPMorgan, a global investment bank. Since 2004, Dr. Pakianathan has served on the board of directors of Alexza Pharmaceuticals, Inc., where she serves as a member of its compensation and nominating and governance committees. Since 2007, Dr. Pakianathan has served on the board of directors of Alder Biopharmaceuticals, Inc. (private), where she serves as a member of its nominating and governance committee, and has served on the board of directors of NeurAxon, Inc. (private), where she serves as a member of its compensation committee. Since 2008, Dr. Pakianathan has served on the board of directors of OncoMed Pharmaceuticals, Inc. a public biopharmaceutical company, where she serves as chair of its audit committee. From 2009 to March 2013, Dr. Pakianathan served on the board of directors of PTC Therapeutics, Inc. Dr. Pakianathan received a B.Sc. from the University of Bombay, India, a M.Sc. from The Cancer Research Institute at the University of Bombay, India, and an M.S. and Ph.D. from Wake Forest University.

Mansoor Raza Mirza M.D. Dr. Mirza has served as a member of Karyopharm's board of directors since October 2010, also serving as a scientific consultant to the company since 2010. Dr. Mirza is Chief Oncologist at the Department of Oncology, Rigshopitalet—the Copenhagen University Hospital, Denmark. Dr. Mirza is both a medical and radiation oncologist, with a primary focus in non-surgical treatment of gynecologic cancers. His other current appointments include service as President-Elect of the Nordic Society of Gynecologic Oncology (NSGO), Medical Director of the NSGO-Clinical Trial Unit, Vice-Chairman of the Danish Gynecological Cancer Society, Founding Executive Member of the European Network of Gynecologic Oncology Trials Group, and membership on the faculty of the European Society of Medical Oncology. He also serves on the board of directors of the Gynecologic Cancer Intergroup, a private organization promoting high quality clinical trials, and Metamark Genetics Inc. (private). He holds a M.D., Diploma in Surgery and Diploma in Clinical Oncology from the Pirogov Moscow State Medical Institute as well as post-graduate education and certification in radiation and medical oncology from the University of Southern Denmark.

Kenneth E. Weg. Mr. Weg has served as a member of Karyopharm's board of directors since February 2013. He has over 34 years of experience in the pharmaceutical industry with global biopharmaceutical companies Bristol-Myers Squibb Company and Merck & Co., Inc. From 1993 to 1998, he was President, Worldwide Medicines Group of Bristol-Myers Squibb, responsible for all ethical pharmaceuticals and over-the-counter medicines on a global basis. Mr. Weg also served as Vice-Chairman of the Board of Bristol-Myers Squibb from 1993 to 1998. He retired from Bristol-Myers Squibb in February 2001. Mr. Weg also served as non-Executive Chairman of Millennium Pharmaceuticals. In addition, he has served as founder and Chairman of Metamark Genetics Inc. He holds a B.A. in English Literature from Dartmouth College and an M.B.A. from Columbia University.

Garen Bohlin. Mr. Bohlin was Executive Vice President of Constellation Pharmaceuticals (private). Previously, he served as Chief Operating Officer of Sirtris Pharmaceuticals. Prior to Sirtris, he was President and Chief Executive Officer of Syntonix Pharmaceuticals (now Biogen Idec). Prior to Syntonix, he was Executive Vice President of Genetics Institute (now Pfizer). Mr. Bohlin played a key strategic role in each of his positions and also had substantial operational experience. Mr. Bohlin currently serves on the board of directors of Acusphere, Inc (private), PreCision Dermatology, Inc. (private) and Tetraphase Pharmaceuticals.

Source: Company website

APPENDIX B – SELECT KARYOPHARM PUBLICATIONS

1. Amzi 2012. Selective Inhibitors of Nuclear Export Block Pancreatic Cancer Cell Proliferation and Reduce Tumor Growth in Mice. Azmi AS, Aboukameel A, Bao B, Sarkar FH, Philip PA, Kauffman M, Shacham S, Mohammad RM. Gastroenterology. 2012 Oct 19. pii: S0016-5085(12)01552-1. doi: 10.1053/j.gastro.2012.10.036.
2. Azmi 2013. Selective inhibitors of nuclear export for the treatment of non-Hodgkin's Lymphomas. Azmi AS, Al-Katib A, Aboukameel A, Mccauley D, Kauffman M, Shacham S, and Mohammad RM; Haematologica. 2013. 98:xxx doi:10.3324/haematol.2012.074781
3. Etchin 2013. Anti-leukemic activity of nuclear export inhibitors that spare normal hematopoietic cells. J Etchin, Q Sun, A Kentsis, A Farmer, ZC Zhang, T Sanda, MR Mansour, C Barcelo, D McCauley, M Kauffman, S Shacham, AL Christie, AL Kung, SJ Rodig, YM Chook and AT Look. Leukemia, 2013. Jan;27(1):66-74.
4. Etchin 2013. KPT-330 inhibitor of CRM1 (XPO1)-mediated nuclear export has selective anti-leukemic activity in preclinical models of T-cell acute lymphoblastic leukemia and acute myeloid leukemia. Etchin J, Sanda T, Mansour MR, Kentsis A, Montero J, Le BT, Christie AL, McCauley D, Rodig SJ, Kauffman M, Shacham S, Stone R, Letai A, Kung AL, Thomas Look A. Br J Hematology. Feb 4. doi: 10.1111.
5. Godley 2012. A drug that stops traffic at the nuclear border. Godley LA. Blood. 2012;1209):1759-60. (This is a very nice mini-review of the Ranganathan paper on AML, described SINE as "a Holy Grail")
6. Inoue 2012. CRM1 Blockade by Selective Inhibitors of Nuclear Export Attenuates Kidney Cancer Growth. Hiromi Inoue, Michael Kauffman, Sharon Shacham, Yosef Landesman, Joy Yang, Christopher P. Evans, Robert H Weiss. Journal of Urology. Online: October, 2012; Publication June 2013.
7. Kalid 2012. Consensus Induced Fit Docking (cIFD): Methodology, Validation, and Application to the Discovery of Novel Crm1 Inhibitors. Ori Kalid, Dora Toledo Warshaviak, Sharon Shechter, Woody Sherman, and Sharon Shacham. 2012. J Comput Aided Mol Des. Nov;26(11):1217-28.
8. Lapolombella 2012. Selective Inhibitors of Nuclear Export (SINE) show that CRM1/XPO1 is a target in Chronic Lymphocytic Leukemia. Lapalombella R, Sun Q, Williams K, Tangeman L, Jha S, Zhong Y, Goettl V, Mahoney E, Berglund C, Gupta S, Farmer A, Mani R, Johnson AJ, Lucas D, Mo X, Daelemans D, Sandanayaka V, Shechter S, McCauley D, Shacham S, Kauffman M, Chook YM, Byrd JC Blood. Nov 29;120(23):4621-34.
9. Muqbil 2013. Understanding XPO1 Target Networks Using Systems Biology and Mathematical Modeling. I. Using Systems Biology and Mathematical Modeling. Muqbil I, Kauffman M, Shacham S, Mohammad RM, Azmi AS. Curr Pharm Des. 2013 Mar 19. [PMID #23530499]
10. Ranganathan 2012. Pre-clinical activity of a novel CRM1 inhibitor in acute myeloid leukemia. Parvathi Ranganathan, Xueyan Yu, Caroline Na, Ramasamy Santhanam, Sharon Shacham, Michael Kauffman, Alison Walker, Rebecca Klisovic, William Blum, Michael Caligiuri, Carlo M. Croce, Guido Marcucci and Ramiro Garzon. Blood. 2012;120(9):1765-1773.
11. Salas Fragomeni RA. CRM1 and BRAF inhibition synergize and induce tumor regression in BRAF mutant melanoma. Salas Fragomeni RA, Chung HW, Landesman Y, Senapedis W, Saint-Martin JR, Tsao H, Flaherty KT, Shacham S, Kauffman M, Cusack JC. Mol Cancer Therapeutics. Apr 24, 2013 [PMID: 23615632]
12. Schmidt 2013. Genome wide studies in Multiple Myeloma identify XPO1/CRM-1 as a critical target validated using the selective nuclear export inhibitor KPT-276. Schmidt J, Braggio E, Mkortuem K, Egan JB, Zhu YX, Xin CS, Tiedemann RE, Palmer SE, Garbitt VM, McCauley D, Kauffman M, Shacham S, Chesi M, Bergsagel PL, Stewart AK. Leukemia. 2013 Jun 11. doi: 10.1038/leu.2013.172. [PMID: 23752175]
13. Tai 2013. CRM1 inhibition induces tumor cell cytotoxicity and impairs osteoclastogenesis in multiple myeloma: molecular mechanisms and therapeutic implications. Tai YT, Landesman Y, Acharya C, Calle Y, Zhong MY, Cea M, Tannenbaum D, Cagnetta A, Reagan M, Munshi AA, Senapedis W, Saint-Martin JR, Kashyap T, Shacham S, Kauffman M, Gu Y, Wu L, Ghobrial I, Zhan F, Kung AL, Schey SA, Richardson P, Munshi NC, Anderson KC. Leukemia. 2013. 2013 Apr 16. doi: 10.1038/leu.2013.115. [PMID 23588715].

14. Turner 2012. Nuclear export of proteins and drug resistance in cancer. Joel G. Turner, Jana Dawson, Daniel M. Sullivan. Biochemical Pharmacology. 2012. Apr 15;83(8):1021-32.

15. Walker 2013. Preclinical and clinical efficacy of XPO1/CRM1 inhibition by the karyopherin inhibitor KPT-330 in Ph + leukemias. Christopher J. Walker, Joshua J. Oaks, Ramasamy Santhanam, Paolo Neviani, Jason G. Harb, Gregory Ferenchak, Justin J. Ellis, Yosef Landesman, Ann-Kathrin Eisfeld, Nash Y. Gabrail, Carrie L. Smith, Michael A. Caligiuri, Peter Hokland, Denis Claude Roy, Alistair Reid, Dragana Milojkovic, John M. Goldman, Jane Apperley, Ramiro Garzon, Guido Marcucci, Sharon Shacham, Michael G. Kauffman and Danilo Perrotti. Blood. 2013. August 22, 2013; doi:10.1182/blood-2013-04-495374.

16. Zhang 2013. Novel Selective Inhibitors of Nuclear Export (SINE) CRM1 Antagonists for Therapy in Mantle Cell Lymphoma. Zhang K, Wang M, Tamayo AT, Shacham S, Kauffman M, Lee J, Zhang L, Ou Z, Li C, Sun L, Ford RJ, Pham LV. Exp Hematol. 2013 Jan;41(1):67-78.

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MARKET OUTPERFORM	Buy	232	*56.45%*	Buy	232	*56.45%*	84	*36.21%*
MARKET PERFORM	Hold	137	*33.33%*	Hold	137	*33.33%*	24	*17.52%*
MARKET UNDERPERFORM	Sell	5	*1.22%*	Sell	5	*1.22%*	0	*0%*
COVERAGE IN TRANSITION		37	*9.00%*		37	*9.00%*	0	*0%*
TOTAL:		411	*100%*		411	*100%*	108	*26.28%*

Stock Price Chart of Rating and Target Price Changes:

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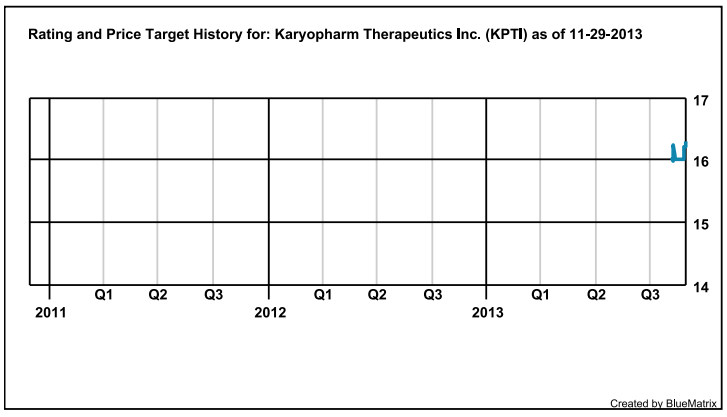

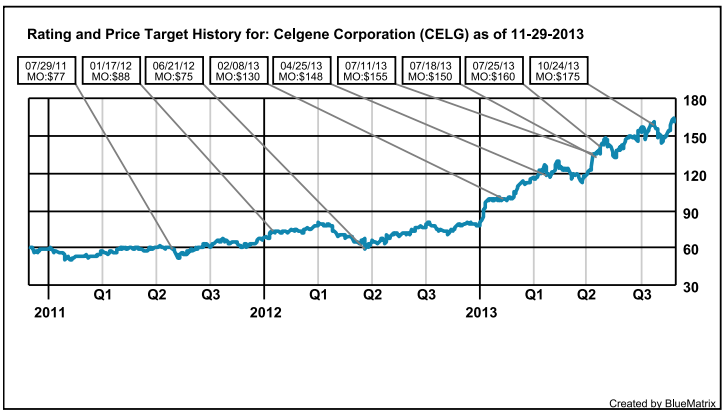

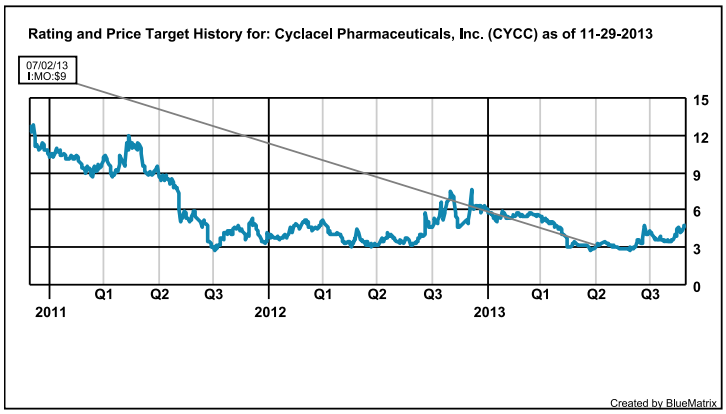

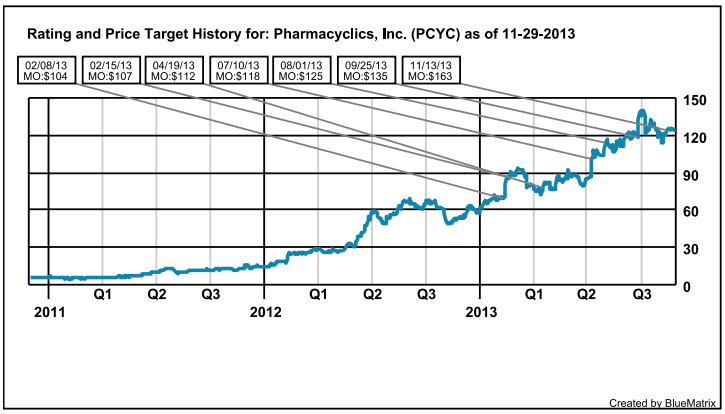

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