January 7, 2014

OUTPERFORM

Reason for report:

COMPANY UPDATE

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LEERINK

EPIZYME, INC.

Objective Responses Enhance Confidence in New Dosing Regimen

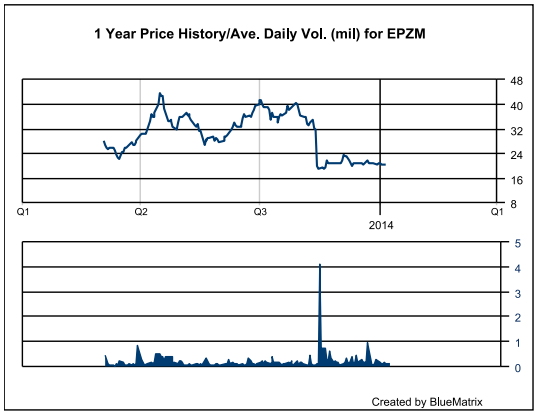
• **Bottom Line:** EPZM achieved proof of concept for the EPZ-5676 DOT1L inhibitor program with a $25M milestone payment from CELG (OP) triggered by objective responses seen in MLL-r (leukemia subtype) patients, as well as $4M development candidate milestone from GSK (MP) for one of the three histone methyltransferase (HMT) targets. The two objective responses were in the previously disclosed 54mg dose cohort after patients were switched from intermittent (21 days on 7 days off) to continuous dosing, and we believe this suggests either the previous dose was sufficiently close or the modified continuous dosing regimen represents a significant improvement. Although patient number is small and duration of response is still unclear, mechanistically, we believe that the responses in this difficult-to-treat patient population are consistent with the epigenetic approach and impressive preclinical data, and bode well for the expansion cohorts at higher doses. While previously released data had demonstrated some activity of EPZ-5676, we believe achieving objective responses represents an important milestone. We are increasing valuation from $25 to $38 to reflect increased probability of success.

• **Response at 54 mg dose is a positive surprise, although duration yet to be seen.** The objective responses (based on working group criteria) were seen in the two fourth dose cohort (54 mg/m2/day) patients who had started on the 21/7 intermittent dosing schedule and were in cycle 2 as of the Nov 14 update. EPZM modified the dosing regimen from 21-day on, 7-day off to 28-day on, aiming to overcome the rebound of biomarker methyl mark during the 7-day drug holiday. Since the modification of the treatment regimen, the remaining two patients on study (1 AML, 1 CMML) continued with the second cycle at 54mg modified dosing. The Dec 9 ASH 2013 investor event slide indicated that they were both in cycle 3; therefore we estimate that they are now in cycle 4. Both continue on treatment, according to management.

• **Responses at lower dose enhance confidence for 80mg+ dosing.** The fifth cohort in the dose escalation portion of the study (originally on 21/7 schedule) is fully enrolled (with 3-4 patients by our estimate). In addition, MLL-r expansion cohorts are enrolling at >= 80 mg dose levels. Objective responses observed from initial two out of two patients with modified dosing regimen were encouraging in this difficult-to-treat patient population, which bodes well for the 80mg+ cohorts, in our view. Mechanistically, longer time continuous treatment with higher dose could maintain continued methyl mark decline, therefore, an improved response. MLL rearrangement (MLL-r) is associated with intermediate to poor prognosis in both AML and ALL. Adult AML patients with MLL-r have 5-year survival of 5-24%. Standard of care treatments limit to intensive chemotherapy and stem cell transplantation.

Key Stats:	**(NASDAQ:EPZM)**
S&P 600 Health Care Index:	**1,272.46**
Price:	**$20.50**
Price Target:	$38.00 from $25.00
Methodology:	NPV, discounted 10% + YE est cash
52 Week High:	$45.72
52 Week Low:	$15.00
Shares Outstanding (mil):	28.4
Market Capitalization (mil):	582.2
Cash Per Share:	$58.58
Dividend (ann):	$0.00
Dividend Yield:	0.0%

General: intra-day price



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2012A	--	--	--	--	$45.2	--	--	--	--	($0.72)	NM
2013E	$8.9A	$14.8A	$8.4A	$8.0	$40.2	($4.27)A	($0.25)A	($0.34)A	($0.39)	($1.81)	NM
2014E	--	--	--	--	$60.0	--	--	--	--	($0.69)	NM
2015E	--	--	--	--	$35.0	--	--	--	--	($1.70)	NM

Source: Company Information and Leerink Partners LLC Research
Revenues in $MM; GAAP EPS

INVESTMENT THESIS

EPZM is a clinical-stage biotechnology company focused on epigenetic treatments for cancer and has a proprietary platform for developing inhibitors of histone methyltransferases (HMTs), an important class of enzymes that controls gene expression. Epigenetics represents an important new direction for new cancer treatment, and EPZM's has a leading platform for development of HMT inhibitors. The historical approach of targeting individual signaling pathways has often yielded modest efficacy except in limited circumstances. This has resulted in pursuit of alternative strategies such as epigenetics, which are supported by impressive survival benefit in a currently marketed epigenetic drug as well as recent findings linking mutations affecting the epigenetic complexes and cancer. HMTs have emerged as an attractive class of epigenetic targets due to both mutational evidence and drugability. EPZM characterized the 96 members of the class, and it has a leading intellectual property position in this area. The company has prioritized 20 HMTs for development and currently has 23 HMTs in screen today. The strong partnerships signed with CELG, GSK and Eisai provide further validation of the platform. One clinical program has shown initial clinical proof of principle and a second could potential report in the near future. Pre-clinical models have demonstrated tumor eradication, without re-growth, post washout of the drug. Though the agent is administered through a continuous IV infusion, our conversation with MEDACorp key opinion leaders (KOLs) suggest that the unmet medical need is high, and if the agent is effective, dosing will not be a problem. EPZ-6438 is an orally dosed inhibitor of EZH2, which is implicated in the development of lymphomas as well as major solid tumors. Preclinical models by both EPZM and GSK have demonstrated the efficacy of EZH2 inhibition in lymphomas, with lack of tumor re-growth, post cessation of dosing. Phase I dosing has recently begun, and an early assessment of efficacy could be available in 1H:14.

Expansion cohorts continue with higher doses, on track to have five clinical developments in 2014. EPZM initiated enrollment of EPZ-5676 expansion cohorts at 80mg+ dosing. Additionally, trials in pediatric MLL-r patients as well as adult MLL-PTD patients could start in 2014. For the EZH2 inhibitor, EPZ-6438, two clinical trials are expected in 2014 including adult NHL as well as pediatric/young adult patients with synovial sarcomas.

GSK milestone marked initial selection of the three HMT candidates. According to the agreement, upon selection of the development candidate, GSK will be solely responsible for subsequent development and commercialization. Additionally, GSK paid fixed amount of research funding during the second and third years of the research term (Jan 2011 – Jan 2015). For 2014, GSK is also obligated to provide full research funding for EPZM on HMT candidates.

EPZ-5676 Dose Escalation -- MLL-r Patient Summary

Cohort Dose	Dx	Treatment Effects as of November 14, 2013	Cycles Completed
2 (24 mg/m2)	**ALL**	**90% circulating blast reduction (no bone marrow aspirate available) Resolution of fevers**	**Cycle 1+**
	AML	None observed	**Cycle 1+**
3 (36 mg/m2)	**AML**	**Maturation in blood and marrow (no change % marrow blasts) Leukocytosis Resolution of cachexia**	**Cycle 3+**
	AML	**Maturation in blood (no change % marrow blasts) Leukocytosis Resolution of leukemia cutis**	**Cycle 2+**
	AML	None observed	**Cycle 1+**
4 (54 mg/m2)	AML	None observed	**Cycle 2+**
	AML	**Maturation in marrow % marrow blast decrease (20%→ 2%)**	**On study (3rd cycle)**
	AML	None observed	Cycle 1+
	CMML[1]	**Under evaluation**	**On study (3rd cycle)**

[1]Extramedullary transformation (skin), t(11;19) detectable in marrow

+Discontinuation due to disease progression

Source: EPZM ASH 2013 investor event presentation

EPZM – Expected Events

Compound	Timing	Event
EPZ-5676	1Q:14	Data from dose escalation expansion cohort in acute leukemia
	1H:14	Initiate Phase I in pediatric MLL-r
	2014	Initiate Phase I in AML with MLL-PTD mutation
EPZ-6438	1H:14	IND filing
	1H:14	Early assessment of therapeutic effects of EPZ-6438 for mutated EZH2 subtype of NHL
	2014	Initiate Phase II clinical trial in NHL with EZH2 mutation
	2014	Initiate Phase I in synovial sarcomas (INI1 deficient tumor)

Source: Company reports and Leerink Partners LLC Research

EPZM – Product Pipeline

Compound	Target	Phase	Partner
EPZ-5676	DOT1L inhibitor	I	CELG
EPZ-6438	EZH2 Inhibitor	I	Eisai
GSK targets	Undisclosed	Pre-clinical	GSK
Platform	Various - 23 HMT in screen today	Pre-clinical	

Source: Company reports

VALUATION

We are increasing our valuation from $25 to $38 for EPZM by assuming increased probability of success for EPZ-5676 and EPZ-6438 as well as higher YE14 cash. We increase our probability of success from 30% to 50% for EPZ-5676 and from 20% to 30% for EPZ-6438. Our $38 valuation is based NPV methodology discounted at 10%. We believe this discount rate is appropriate as we use probability-weighted sales for the products and we lowered the discount rate to be consistent with what we currently use for other companies in our coverage universe due to greater market risk tolerance. We include $85M of cash (vs. prior $60M) at the end of 2014 and $500M in technology value.

RISKS TO VALUATION

- Pre-clinical models may not accurately predict for clinical benefit.
- Human safety and efficacy of EPZ-5676 or EPZ-6438 are unknown due to early stage of development. Dosing of EPZ-5676 (continuous infusion) is not optimal, and human dosing requirement of EPZ-6438 remains to be determined.
- Competition from GSK or other companies focused on these targets could negatively impact EPZM's revenues.
- Competition from other agents for MLL-r or other hematological malignancies could limit the revenues of EPZM's products.
- Commercial uptake may be limited by reimbursement, access or dosing concerns for EPZ-5676 and EPZ-6438.

Figures in $000, except EPS	2011A	2012A	1QA	2QA	3QA	4QE	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
EPZ-5676																
US											6,753	62,552	123,760	170,843	230,779	338,118
EU											0	7,028	56,341	100,932	164,122	215,866
JP											0	0	1,114	8,908	18,153	25,842
Total											6,753	69,580	181,214	280,684	413,053	579,826
Probability of success											*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*
OUS Royalty Rate												*5.0%*	*5.0%*	*6.0%*	*7.0%*	*8.0%*
EPZ-6438																
US											0	23,725	219,752	431,736	587,653	846,568
EU											0	0	13,627	122,900	236,425	316,887
JP											0	0	0	1,644	14,800	29,569
Total											0	23,725	233,379	556,280	838,877	1,193,024
Probability of success											*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*
OUS Royalty Rate												*6.0%*	*6.0%*	*6.0%*	*6.0%*	*6.0%*
Booked by Epizyme																
EPZ-5676 US (POS adjusted)											2,026	18,766	37,128	51,253	69,234	101,435
EPZ-6438 US (POS adjusted) - 50% share											0	2,372	21,975	43,174	58,765	84,657
Sales booked by other companies																
EPZ-5676 (POS adjusted)											0	2,108	17,236	32,952	54,682	72,512
EPZ-6438 (POS adjusted)											0	0	2,725	24,909	50,245	69,291
Royalties																
EPZ-5676 (POS adjusted)											0	105	862	1,977	3,828	5,801
EPZ-6438 (POS adjusted)											0	0	164	1,495	3,015	4,157
Collaboration revenue	6,944	45,222	8,882	14,839	8,444	8,000	40,165	60,000	35,000	20,000	20,000	20,000	0	0	0	0
Total revenues			8,882	14,839	8,444	8,000	40,165	60,000	35,000	20,000	22,026	41,244	60,129	97,898	134,841	196,051
Operating expenses:																
Research and development	22,911	38,482	13,361	13,937	14,584	15,000	56,882	65,000	70,000	70,000	70,000	70,000	70,000	70,000	70,000	70,000
General and administrative	5,000	7,508	2,998	3,079	3,587	4,000	13,664	15,000	15,000	15,000	35,000	50,000	50,000	50,000	50,000	50,000
Total operating expenses	27,911	45,990	16,359	17,016	18,171	19,000	70,546	80,000	85,000	85,000	105,000	120,000	120,000	120,000	120,000	120,000
Loss from operations	(20,967)	(768)	(7,477)	(2,177)	(9,727)	(11,000)	(30,381)	(20,000)	(50,000)	(65,000)	(82,974)	(78,756)	(59,871)	(22,102)	14,841	76,051
Other income (expense):																
Interest income	33	145	19	20	0	20	59	59	59	59	59	59	59	59	59	59
Other expense	(23)	(78)	(39)	(55)	23	(40)	(111)	(111)	(111)	(111)	(111)	(111)	(111)	(111)	(111)	(111)
Other income (expense), net	10	67	(20)	(35)	23	(20)	(52)	(52)	(52)	(52)	(52)	(52)	(52)	(52)	(52)	(52)
Loss before income taxes	(20,957)	(701)	(7,497)	(2,212)	(9,704)	(11,020)	(30,433)	(20,052)	(50,052)	(65,052)	(83,026)	(78,808)	(59,923)	(22,154)	14,789	75,999
Income tax expense	—	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Net income	(20,957)	(702)	(7,497)	(2,212)	(9,704)	(11,020)	(30,433)	(20,052)	(50,052)	(65,052)	(83,026)	(78,808)	(59,923)	(22,154)	14,789	75,999
Less: accretion of redeemable convertible preferred stock to redemption value	45	486	157	107	0	0	264	0	0	0	0	0	0	0	0	0
Loss attributable to common stockholders	(21,002)	(1,188)	(7,654)	(2,319)	(9,704)	(11,020)	(30,697)	(20,052)	(50,052)	(65,052)	(83,026)	(78,808)	(59,923)	(22,154)	14,789	75,999
Loss per share attributable to common stockholders:																
Basic	($14.65)	($0.72)	($4.27)	($0.25)	($0.34)	($0.39)	($1.81)	($0.69)	($1.70)	($2.18)	($2.74)	($2.56)	($1.92)	($0.70)	$0.46	$2.33
Diluted	($14.65)	($0.72)	($4.27)	($0.25)	($0.34)	($0.39)	($1.81)	($0.69)	($1.70)	($2.18)	($2.74)	($2.56)	($1.92)	($0.70)	$0.40	$2.00
Weighted average shares outstanding:																
Basic	1,434	1,645	1,791	9,146	28,406	28,406	16,937	28,974	29,409	29,850	30,298	30,752	31,213	31,682	32,157	32,639
Diluted	1,434	1,645	1,791	13,797	32,985	33,018	20,398	33,678	34,184	34,696	35,217	35,745	36,281	36,825	37,378	37,938

Source: Company information and Leerink Swann estimates

Disclosures Appendix

Analyst Certification

I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

Valuation

Our price target is $38 for EPZM, which assumes probability of success for EPZ-5676 and EPZ-6438 as well as higher YE14 cash. Our probability of success is 50% for EPZ-5676 and 30% for EPZ-6438. Our $38 valuation is based NPV methodology discounted at 10%. We believe this discount rate is appropriate as we use probability-weighted sales for the products and we lowered the discount rate to be consistent with what we currently use for other companies in our coverage universe due to greater market risk tolerance. We include $85M of cash at the end of 2014 and $500M in technology value.

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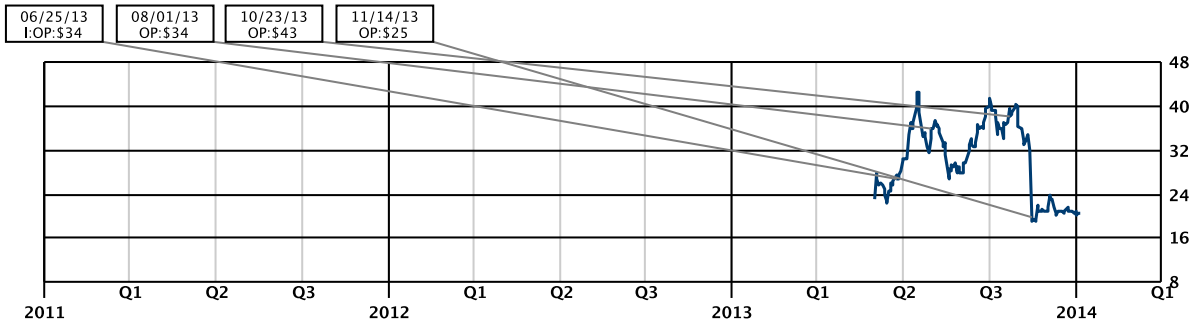
Rating and Price Target History for: Epizyme, Inc. (EPZM) as of 01-06-2014



On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

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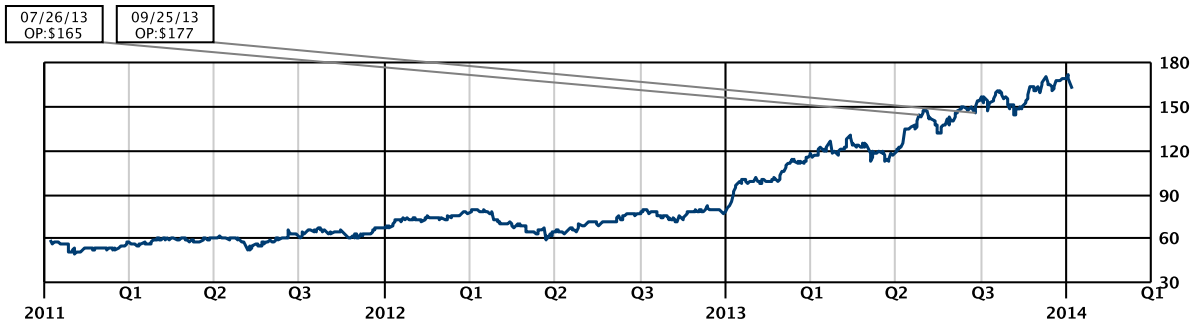
Rating and Price Target History for: Celgene, Inc. (CELG) as of 01-06-2014



Leerink Swann initiated coverage of CELG with an Outperform rating on February 7, 2003. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

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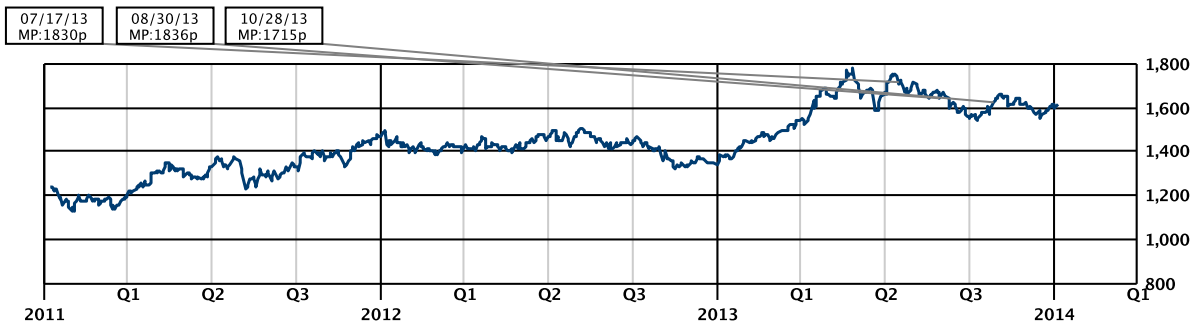
Rating and Price Target History for: GlaxoSmithKline plc (GSK LN) as of 01-06-2014



Leerink Swann initiated coverage of GSK LN with a Market Perform rating on Nov. 24, 2009. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

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			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	111	64.90	27	24.00
HOLD [MP]	60	35.10	0	0.00
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): **We expect this stock to outperform its benchmark over the next 12 months.**

Market Perform (Hold/Neutral): **We expect this stock to perform in line with its benchmark over the next 12 months.**

Underperform (Sell): **We expect this stock to underperform its benchmark over the next 12 months.The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.**

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

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In the past 12 months, the Firm has received compensation for providing investment banking services to Epizyme, Inc. .

Leerink Partners LLC makes a market in Epizyme, Inc. and Celgene, Inc.

Leerink Partners LLC is willing to sell to, or buy from, clients the common stock of GlaxoSmithKline plc on a principal basis.

In the past 12 months, an affiliate of the Firm, Leerink Swann Consulting LLC, has received compensation for providing non-securities services to: Celgene, Inc. and GlaxoSmithKline plc.

Leerink Partners LLC has acted as the manager for a public offering of Epizyme, Inc. in the past 12 months.

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