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Reason for report:

COMPANY UPDATE

EPIZYME, INC.

EPZ-5676 Has Activity but Dosing Needs to Be Optimized

• **Bottom Line:** EPZM announced data from the dose escalation cohorts of Phase I of EPZ-5676 (DOT1L) this morning. The data show activity and clinical benefit of EPZ-567; however using the current dosing regimen and at the current dose levels, EPZ-5676 monotherapy appeared not sufficiently effective in preventing disease progression. The initial encouraging activity seen at a low dose reported previously in an MLL-r ALL patient did not appear to improve in two higher dose cohorts although all evaluable MLL-r patients at the higher doses were AML patients. The stock reaction was likely exacerbated by concerns over lock-up expiration on 11/26. We believe it is too early to write off EPZ-5676 as we believe there remain other shots on goal either with optimized dosing or in combination with other agents. We remain OP-rated, but are lowering valuation from \$43 to \$25.

• **The drug is clearly doing something but appears unable to keep patients from progression using the current dosing.** Evidence of activity of EPZ-5676 in 4/8 MLL-r patients includes reduction in blast count, maturation of leukemic blasts, and resolution of leukemia cutis. On the other hand, essentially all MLL-r patients (except one) have progressed within 1-3 cycles including 3 of the 4 patients in whom some treatment effect was observed. The response of 90% circulating blast reduction seen at 24 mg/m² did not seem to have improved or even to have maintained in most of the patients receiving 36 mg/m² or 54 mg/m². The numbers are too small to draw a conclusion but latter patients were AML patients vs. ALL for the first patient who had shown activity.

• **The dose and regimen are far from optimized.** The company reported a significant rebound of biomarker methyl mark during the 7-day drug holiday in the current 21-day on 7-day off cycle. According to the company, methyl mark reduction was consistently observed at doses 36 mg/m² or higher and is dose-dependent. There has not been any significant toxicity concern; therefore there appears to be room to optimize dosing. The company is currently enrolling an 80 mg/m² cohort and will test 80 mg/m² without a drug holiday. As MLL-r leukemias have such an aggressive disease, the combination with chemotherapy could be a better strategy.



LEERINK SWANN

HEALTHCARE EQUITY RESEARCH

Key Stats:

(NASDAQ:EPZM)

S&P 600 Health Care Index: 1,248.53

Price: \$18.95

Price Target: \$25.00 from \$43.00

Methodology: NPV, discounted at 10%

52 Week High: \$45.72

52 Week Low: \$15.00

Shares Outstanding (mil): 1.7

Market Capitalization (mil): 32.2

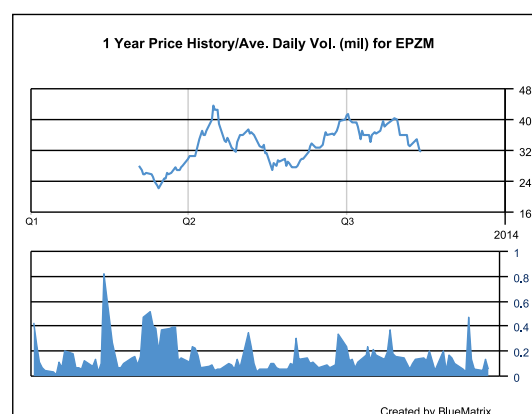
Book Value/Share: 0.00

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 Swann 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 is 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. Two clinical programs could potentially generate proof of principle data in the near future. EPZ-5676 is a DOT1L inhibitor for the treatment of MLL-r, a subtype of leukemias with particularly poor prognosis. 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.



EPZM – Expected Events

Compound	Timing	Event
EPZ-5676	4Q:13	Initiate expansion cohort of EPZ-5676 in MLL-r leukemias
	4Q:13	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 Swann LLC

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 lowering our valuation from \$43 to \$25 for EPZM by assuming reduced probability of success for EPZ-5676 and EPZ-6438. We lower our probability of success from 50% to 30% for EPZ-5676 and from 40% to 20% for EPZ-6438. Our \$25 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 \$60M of cash 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
<i>Total</i>											6,753	69,580	181,214	280,684	413,053	579,826
<i>Probability of success</i>											30.0%	30.0%	30.0%	30.0%	30.0%	30.0%
<i>OUS Royalty Rate</i>												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
<i>Total</i>											0	23,725	233,379	556,280	838,877	1,193,024
<i>Probability of success</i>											20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
<i>OUS Royalty Rate</i>												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

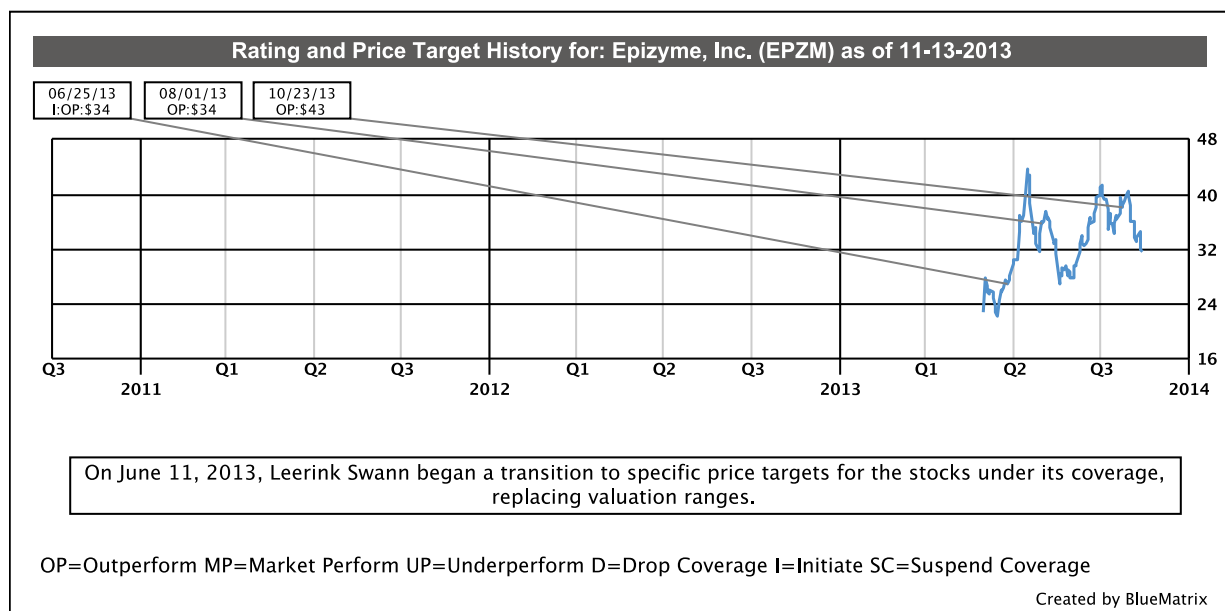
I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

Valuation

Our valuation is \$25 for EPZM by assuming reduced probability of success for EPZ-5676 and EPZ-6438. We lower our probability of success from 50% to 30% for EPZ-5676 and from 40% to 20% for EPZ-6438. Our \$25 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 \$60M of cash at the end of 2014 and \$500M in technology value.

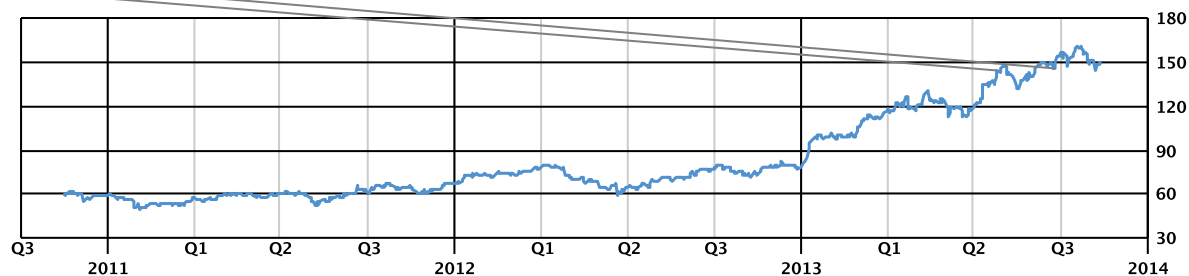
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Rating and Price Target History for: Celgene, Inc. (CELG) as of 11-13-2013

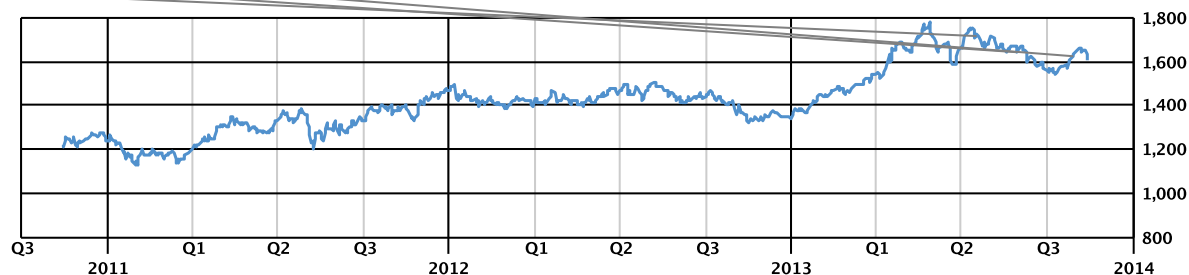
07/26/13
OP:\$16509/25/13
OP:\$177

Leerink Swann initiated coverage of CELG with an Outperform rating on February 7, 2009. 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

Created by BlueMatrix

Rating and Price Target History for: GlaxoSmithKline plc (GSK LN) as of 11-13-2013

07/17/13
MP:1830p08/30/13
MP:1836p10/28/13
MP:1715p

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.

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

Created by BlueMatrix



Distribution of Ratings/Investment Banking Services (IB) as of 09/30/13				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			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.

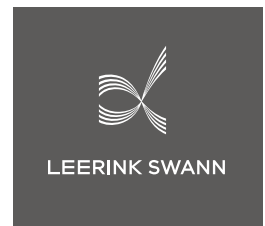
Important Disclosures

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Leerink Swann Consulting LLC, an affiliate of Leerink Swann LLC, is a provider of evidence-based strategy and consulting to the healthcare industry.

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



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

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

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