

Reason for report:

EARNINGS

EPIZYME, INC.

On-Track Development -- Clinical Catalysts to Return in 2H:14

• **Bottom Line:** On the 1Q:14 earnings call, EPZM highlighted on-track clinical development and reaffirmed YE:14 cash guidance of \$170M. Both epigenetic candidates EPZ-5676 (DOT1L inhibitor) and EPZ-6438 (EZH2 inhibitor) programs are on track to deliver Phase I data and advance to Phase II or pivotal trials in 2014. Recent initiation of the EPZ-5676 Phase I trial in pediatric MLL-r acute leukemias marks a full-speed clinical development for EPZM's lead compound in three indications. Data for both EPZ-5676 and EPZ-6438, which may be more important for EPZM, are expected in 2H, including some potentially before ASH in December. Following initial clinical proof-of-concept data for EPZ-5676 in difficult-to-treat MLL-r acute leukemias, good progress has been made in all three EPZM programs in DOT1L and EZH2 inhibitors and the GSK (MP) partnership, and there is continued validation of the epigenetics approach for cancer drug development. As multiple clinical data readouts return in 2H, we see EPZM gaining greater visibility and interest. Our valuation remains \$38.

• **Clinical development on track, two Phase I data presentations at medical conferences in 2014.** EPZM recently initiated the EPZ-5676 (DOT1L inhibitor) Phase Ib dose escalation trial in pediatric MLL-r acute leukemias. Enrollment for the expansion cohorts in both MLL-r and MLL-PTD adult patients is ongoing with data (for both escalation and expansion cohorts) expected in 2H:14. Assuming a positive readout, management plans to meet with the FDA to discuss the potential registration trial. Data from EPZ-6438 Phase I dose escalation studies in hematologic and solid tumors are also expected in 2H:14, and Phase II proof-of-concept trials in NHL and synovial sarcomas will be initiated in 2014 upon completion of the Phase I trials.

• **Additional milestones expected for 2014.** EPZM earned \$6M from GSK through April 2014 for completing the selection of all three collaboration targets. EPZM could also gain a \$10M milestone from Eisai for initiating a Phase II proof-of-concept trial for EPZ-6438 in 2014.

• **Model update.** For 1Q:14, EPZM reported \$13.4M in revenue vs. our estimate of \$10.0M. Operating expenses were \$20.3M vs. our estimate of \$23.8M. Dilutive EPS was (\$0.22) vs. our estimate of (\$0.43). The company reaffirmed YE:14 cash of \$170M and guided that it should support operations through at least mid-2016. We update our model to reflect these changes. As a result, our 2014 revenue estimate changes from \$40.0M to \$43.4M, and EPS changes from (\$1.71) to (\$1.59).

Key Stats:

(NASDAQ:EPZM)

S&P 600 Health Care Index:	1,225.55
Price:	\$22.29
Price Target:	\$38.00
Methodology:	NPV analysis
52 Week High:	\$45.72
52 Week Low:	\$15.00
Shares Outstanding (mil):	31.0
Market Capitalization (mil):	691.0
Cash Per Share:	\$7.66
Dividend (ann):	\$0.00
Dividend Yield:	0.0%



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2013A	\$8.9	\$14.8	\$8.4	\$36.3	\$68.5	(\$4.27)	(\$0.25)	(\$0.34)	\$0.52	(\$0.22)	NM
2014E - New	\$13.4A	\$10.0	\$10.0	\$10.0	\$43.4	(\$0.22)A	(\$0.45)	(\$0.45)	(\$0.46)	(\$1.59)	NM
2014E - Old	\$10.0	\$10.0	\$10.0	\$10.0	\$40.0	(\$0.43)	(\$0.43)	(\$0.43)	(\$0.43)	(\$1.71)	NM
2015E - New	--	--	--	--	\$35.0	--	--	--	--	(\$2.06)	NM
2015E - Old	--	--	--	--	\$35.0	--	--	--	--	(\$2.08)	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 potentially 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.

EPZM – Expected Events

<u>Compound</u>	<u>Timing</u>	<u>Event</u>
EPZ-5676 (DOT1Li)	2H:14	Data at a medical conference from Phase I dose escalation and expansion cohort in AML with MLL-r and MLL-PTD mutation
EPZ-6438 (EZH2i)	2014	Initiate POC Phase II clinical trial in NHL with EZH2 mutation
	2014	Initiate POC Phase II in synovial sarcomas (INI1 deficient tumor)
	2H:14	Data at a medical conference from Phase I dose escalation study

Source: Company reports and Leerink Partners LLC Research

EPZM – Product Pipeline

<u>Compound</u>	<u>Target</u>	<u>Phase</u>	<u>Partner</u>
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

Our price target for EPZM is \$38. Our probability of success is 50% for EPZ-5676 and 30% for EPZ-6438. Our \$38 price target is based on 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 \$170M 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.

EPZM Income Statement (Figures in \$000, except EPS)	2012A	2013A	1QA	2QE	3QE	4QE	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
EPZ-5676														
US										6,753	62,552	123,760	170,843	230,779
EU										0	7,028	56,341	100,932	164,122
JP										0	0	1,114	8,908	18,153
Total										6,753	69,580	181,214	280,684	413,053
Probability of success										30.0%	30.0%	30.0%	30.0%	30.0%
OUS Royalty Rate											5.0%	5.0%	6.0%	7.0%
EPZ-6438														
US										0	23,725	219,752	431,736	587,653
EU										0	0	13,627	122,900	236,425
JP										0	0	0	1,644	14,800
Total										0	23,725	233,379	556,280	838,877
Probability of success										20.0%	20.0%	20.0%	20.0%	20.0%
OUS Royalty Rate											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
EPZ-6438 US (POS adjusted) - 50% share										0	2,372	21,975	43,174	58,765
Sales booked by other companies														
EPZ-5676 (POS adjusted)										0	2,108	17,236	32,952	54,682
EPZ-6438 (POS adjusted)										0	0	2,725	24,909	50,245
Royalties														
EPZ-5676 (POS adjusted)										0	105	862	1,977	3,828
EPZ-6438 (POS adjusted)										0	0	164	1,495	3,015
Collaboration revenue	45,222	68,482	13,391	10,000	10,000	10,000	43,391	35,000	20,000	20,000	20,000	0	0	0
Total revenues		68,482	13,391	10,000	10,000	10,000	43,391	35,000	20,000	22,026	41,244	60,129	97,898	134,841
Operating expenses:														
Research and development	38,482	57,567	15,347	19,700	19,900	20,000	74,947	75,000	75,000	75,000	75,000	75,000	75,000	75,000
Stock based compensation			750	750	750	750	3,000	3,000	3,000	3,000	3,000	3,000	3,000	3,000
General and administrative	7,508	14,042	4,956	5,000	5,000	5,000	19,956	25,000	30,000	35,000	50,000	50,000	50,000	50,000
Stock based compensation			1,375	1,375	1,375	1,375	5,500	5,555	6,000	7,000	8,500	8,500	8,500	8,500
Total operating expenses	45,990	71,609	20,303	24,700	24,900	25,000	94,903	103,000	108,000	113,000	128,000	128,000	128,000	128,000
Loss from operations	(768)	(3,127)	(6,912)	(14,700)	(14,900)	(15,000)	(51,512)	(68,000)	(88,000)	(90,974)	(86,756)	(67,871)	(30,102)	6,841
Interest income	145	39	28	0	0	0	28	28	28	28	28	28	28	28
Other expense	(78)	(46)	0	0	0	0	0	0	0	0	0	0	0	0
Other income (expense), net	67	(7)	28	0	0	0	28	28	28	28	28	28	28	28
Loss before income taxes	(701)	(3,134)	(6,884)	(14,700)	(14,900)	(15,000)	(51,484)	(67,972)	(87,972)	(90,946)	(86,728)	(67,843)	(30,074)	6,869
Income tax expense	1	349	0	0	0	0	0	0	0	0	0	0	0	0
Income before preferred stock holders	(702)	(3,483)	(6,884)	(14,700)	(14,900)	(15,000)	(51,484)	(67,972)	(87,972)	(90,946)	(86,728)	(67,843)	(30,074)	6,869
Income to preferred stock holders	486	268	0	0	0	0	0	0	0	0	0	0	0	0
Net income - GAAP	(1,188)	(3,751)	(6,884)	(14,700)	(14,900)	(15,000)	(51,484)	(67,972)	(87,972)	(90,946)	(86,728)	(67,843)	(30,074)	6,869
Stock based compensation			2,125	2,125	2,125	2,125	8,500	8,555	9,000	10,000	11,500	11,500	11,500	11,500
Net income - Non-GAAP			(4,759)	(12,575)	(12,775)	(12,875)	(42,984)	(59,417)	(78,972)	(80,946)	(75,228)	(56,343)	(18,574)	18,369
EPS - GAAP														
Basic	(\$0.72)	(\$0.22)	(\$0.22)	(\$0.45)	(\$0.45)	(\$0.46)	(\$1.59)	(\$2.06)	(\$2.63)	(\$2.68)	(\$2.52)	(\$1.94)	(\$0.85)	\$0.19
Diluted	(\$0.72)	(\$0.22)	(\$0.22)	(\$0.45)	(\$0.45)	(\$0.46)	(\$1.59)	(\$2.06)	(\$2.63)	(\$2.68)	(\$2.52)	(\$1.94)	(\$0.85)	\$0.18
Weighted average shares outstanding:														
Basic	1,645	17,049	30,959	32,900	32,933	32,966	32,439	32,926	33,420	33,921	34,430	34,946	35,471	36,003
Diluted	1,645	19,869	33,779	34,454	34,799	35,147	34,544	35,063	35,589	36,122	36,664	37,214	37,772	38,339

Source: Company information and Leerink estimates

Disclosures Appendix

Analyst Certification

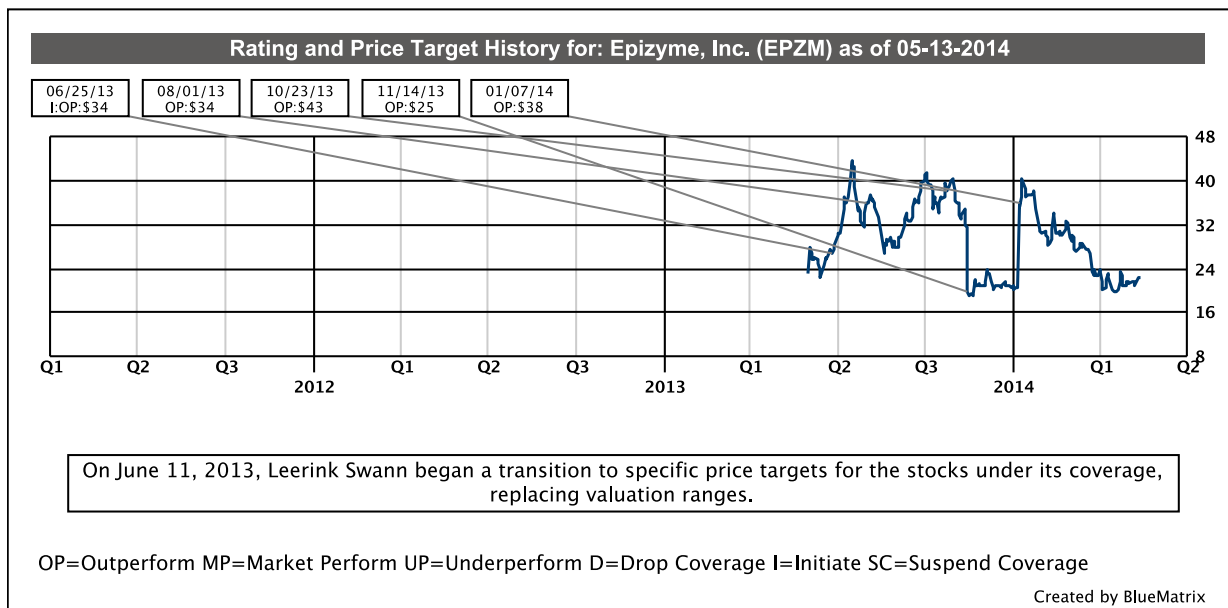
I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

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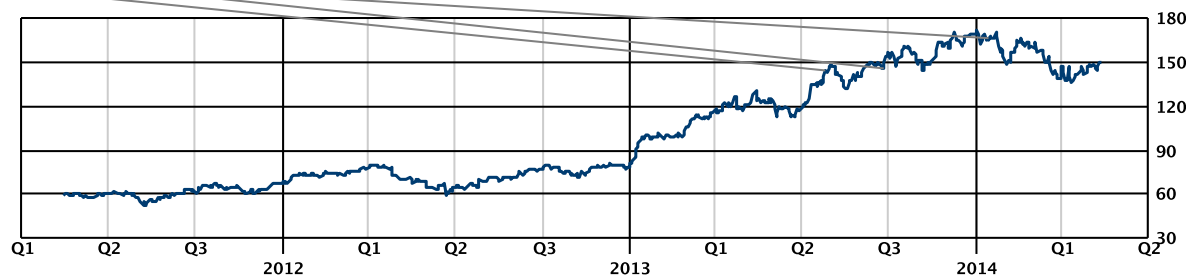


Rating and Price Target History for: Celgene, Inc. (CELG) as of 05-13-2014

07/26/13
OP:\$165

09/25/13
OP:\$177

01/14/14
OP:\$197



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.

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

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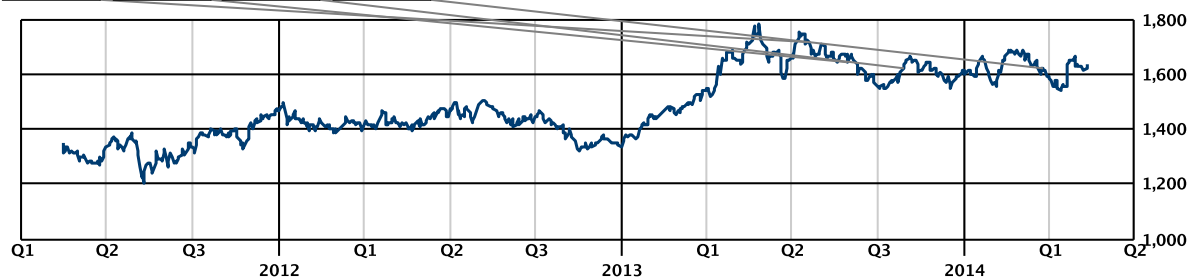
Rating and Price Target History for: GlaxoSmithKline plc (GSK LN) as of 05-13-2014

07/17/13
MP:1830p

08/30/13
MP:1836p

10/28/13
MP:1715p

03/26/14
MP:1654p



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

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Distribution of Ratings/Investment Banking Services (IB) as of 03/31/14				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	131	68.23	46	35.11
HOLD [MP]	61	31.77	3	4.92
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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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.

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

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