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Reason for report:

EARNINGS

## EPIZYME, INC.

## Two Clinical Candidates Progressing Toward Near-term Proof of Principle Data

• **Bottom Line:** EPZM's first quarterly report as a public company was relatively uneventful but highlighted two clinical-stage epigenetic candidates that are expected to report first clinical data from dose-escalation studies in 2H:13 (EPZ-5676, DOT1L inhibitor) and 2014 (EPZ-6438, EZH2 inhibitor) followed by expansion cohorts in selected patients that will provide the initial test of efficacy. Given the strong preclinical data and high level of interest in targeting epigenetics for cancer drug development, we expect heightened interest in these early proof of principle data, which if positive could further increase the interest in the platform. Financially, EPZM is well positioned with available cash projected to support operations into 2015. We are increasing our valuation from \$34 to \$43 by assigning a higher valuation to EPZM's technology platform in part due to an improved market environment for biotech platform companies.

• **Enrollment of lead candidate EPZ-5676 in Phase I has been expanded from one to five clinical sites.** The dose escalation phase continues and understandably management does not plan to give a patient-by-patient update, and data will be described at the end of the escalation period expected to be in 2H:13. Previously, at the time of its IPO, the company had disclosed dosing of four patients including one with MLL rearrangement who showed signs of clinical response (90% reduction in circulating leukemic blast count) to EPZ-5676 at the second dose level.

• **Preclinical EPZ-5676 data were recently published in *Blood* showing complete and sustained regression in a rat xenograft model of MLL-rearranged leukemia -- dose relationship may have clinical read-through.** Daigle et al. (*Blood* 2013, published online on June 25) examined EPZM's lead clinical candidate. The anti-tumor effect was shown to be highly dose- and schedule-dependent, and optimal activity was achieved by continuous IV infusion for a period of 14 days or longer. This would appear to suggest that the initial clinical activity could be substantially improved as the dose is increased.

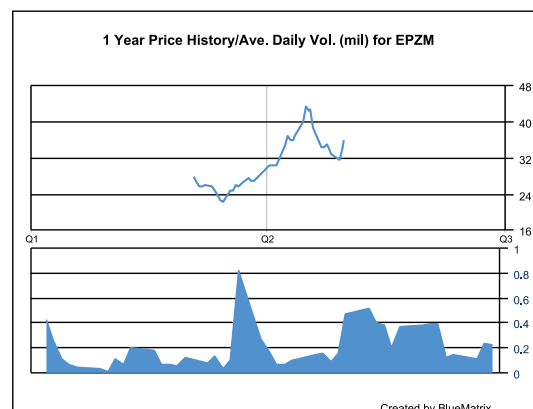
• **Second candidate EPZ6438 (EZH2 inhibitor) is in clinic, and there appears to be no toxicity limitations on dose exploration.** Upon completion of dose escalation (expected in 2014), the company plans an update as well as initiation of an expansion cohort in patients with point mutations in EZH2.



## Key Stats:

(NASDAQ:EPZM)

<b>S&amp;P 600 Health Care Index:</b>	<b>1,102.35</b>
<b>Price:</b>	<b>\$36.10</b>
Price Target:	\$43.00 from \$34.00
Methodology:	DCF analysis
52 Week High:	\$45.72
52 Week Low:	\$15.00
Shares Outstanding (mil):	28.4
Market Capitalization (mil):	1,025.2
Book Value/Share:	0.00
Cash Per Share:	\$5.23
Dividend (ann):	\$0.00
Dividend Yield:	0.0%



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2012A	--	--	--	--	\$45.2	--	--	--	--	(\$0.72)	NM
2013E - New	\$8.9A	\$14.8A	\$9.0	\$10.0	\$42.7	(\$4.27)A	(\$0.25)A	(\$0.32)	(\$0.28)	(\$1.59)	NM
2013E - Old	\$8.9A	\$13.0	\$9.0	\$10.0	\$40.8	(\$4.27)A	(\$2.80)	(\$0.32)	(\$0.28)	(\$1.97)	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. Biological activity was seen in the 1st MLL-r patient dosed in the Phase I dose escalation, with a decrease in blast counts prior to CNS relapse. 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. Early efficacy data from the trial will be available in 2H:13. 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 will be available in 1H:14.

**Financial results highlight strong cash position.** EPZM reported generally in-line financial results for 2Q:13, with slightly better top-line collaboration revenue (\$14.8M vs. our estimate of \$13M) and lower operating expenses (\$17M vs. our estimate of \$18M). Due to the difference in share count estimates, the EPS comparison is not meaningful. Management projects operating cash burn of ~\$65M and ending 2013 with \$115M in cash, which is expected to fund the company through at least mid-2015 and proof of principle data on the lead compounds. We updated our model to reflect 2Q results.



### EPZM – Expected Events

Timing	Event
2H:13	Early assessment of therapeutic effects of EPZ-5676 in MLL-r leukemias
2H:13	Initiate expansion cohort of EPZ-5676
1H:14	Early assessment of therapeutic effects of EPZ-6438 for mutated EZH2 subtype of NHL
2014	Initiate Phase II clinical trial of EPZ-6438

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 increasing our valuation of EPZM from \$34 to \$43 by assigning more valuation to EPZM's technology platform due to greater market acceptance and generally higher valuation placed on biotech platform companies. Our valuation on EPZM is based on a DCF for EPZ-5676 and EPZ-6438 discounted at 10% (vs. 11% previously). 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 also include \$60M of cash at the end of 2014 and \$500M in technology value (vs. \$300M previously). Our previous valuation of \$34 was based on a similar DCF analysis with changes noted above.

## 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

EPZ-5676

US

EU

JP

*Total**Probability of success**OUS Royalty Rate*EPZ-6438

US

EU

JP

*Total**Probability of success**OUS Royalty Rate*Booked by Epizyme

EPZ-5676 US (POS adjusted)

EPZ-6438 US (POS adjusted) - 50% share

Sales booked by other companies

EPZ-5676 (POS adjusted)

EPZ-6438 (POS adjusted)

Royalties

EPZ-5676 (POS adjusted)

EPZ-6438 (POS adjusted)

	2011A	2012A	1QA	2QA	3QE	4QE	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
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>											50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
<i>OUS Royalty Rate</i>												5.0%	5.0%	6.0%	7.0%	8.0%
<u>EPZ-6438</u>																
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>											40.0%	40.0%	40.0%	40.0%	40.0%	40.0%
<i>OUS Royalty Rate</i>												6.0%	6.0%	6.0%	6.0%	6.0%
<u>Booked by Epizyme</u>																
EPZ-5676 US (POS adjusted)											3,377	31,276	61,880	85,422	115,389	169,059
EPZ-6438 US (POS adjusted) - 50% share											0	4,745	43,950	86,347	117,531	169,314
<u>Sales booked by other companies</u>																
EPZ-5676 (POS adjusted)											0	3,514	28,727	54,920	91,137	120,854
EPZ-6438 (POS adjusted)											0	0	5,451	49,818	100,490	138,583
<u>Royalties</u>																
EPZ-5676 (POS adjusted)											0	176	1,436	3,295	6,380	9,668
EPZ-6438 (POS adjusted)											0	0	327	2,989	6,029	8,315
Collaboration revenue	6,944	45,222	8,882	14,839	9,000	10,000	42,721	60,000	35,000	20,000	20,000	20,000	0	0	0	0
Total revenues			8,882	14,839	9,000	10,000	42,721	60,000	35,000	20,000	23,377	56,197	107,594	178,053	245,329	356,356
Operating expenses:																
Research and development	22,911	38,482	13,361	13,937	15,000	15,000	57,298	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	3,000	3,000	12,077	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	18,000	18,000	69,375	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)	(9,000)	(8,000)	(26,654)	(20,000)	(50,000)	(65,000)	(81,623)	(63,803)	(12,406)	58,053	125,329	236,356
Other income (expense):																
Interest income	33	145	19	20	20	20	79	79	79	79	79	79	79	79	79	79
Other expense	(23)	(78)	(39)	(55)	(40)	(40)	(174)	(174)	(174)	(174)	(174)	(174)	(174)	(174)	(174)	(174)
Other income (expense), net	10	67	(20)	(35)	(20)	(20)	(95)	(95)	(95)	(95)	(95)	(95)	(95)	(95)	(95)	(95)
Loss before income taxes	(20,957)	(701)	(7,497)	(2,212)	(9,020)	(8,020)	(26,749)	(20,095)	(50,095)	(65,095)	(81,718)	(63,898)	(12,501)	57,958	125,234	236,261
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)	(9,020)	(8,020)	(26,749)	(20,095)	(50,095)	(65,095)	(81,718)	(63,898)	(12,501)	57,958	125,234	236,261
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)	(9,020)	(8,020)	(27,013)	(20,095)	(50,095)	(65,095)	(81,718)	(63,898)	(12,501)	57,958	125,234	236,261
Loss per share attributable to common stockholders:																
Basic	(\$14.65)	(\$0.72)	(\$4.27)	(\$0.25)	(\$0.32)	(\$0.28)	(\$1.59)	(\$0.69)	(\$1.70)	(\$2.18)	(\$2.70)	(\$2.08)	(\$0.40)	\$1.83	\$3.89	\$7.24
Diluted	(\$14.65)	(\$0.72)	(\$4.27)	(\$0.25)	(\$0.32)	(\$0.28)	(\$1.59)	(\$0.69)	(\$1.70)	(\$2.18)	(\$2.70)	(\$2.08)	(\$0.40)	\$1.58	\$3.35	\$6.23
Weighted average shares outstanding:																
Basic	1,434	1,645	1,791	9,146	28,414	28,414	16,941	28,982	29,417	29,858	30,306	30,761	31,222	31,690	32,166	32,648
Diluted	1,434	1,645	1,791	9,146	32,985	32,985	19,227	33,645	34,149	34,662	35,182	35,709	36,245	36,789	37,340	37,901

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

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### Risks to Valuation

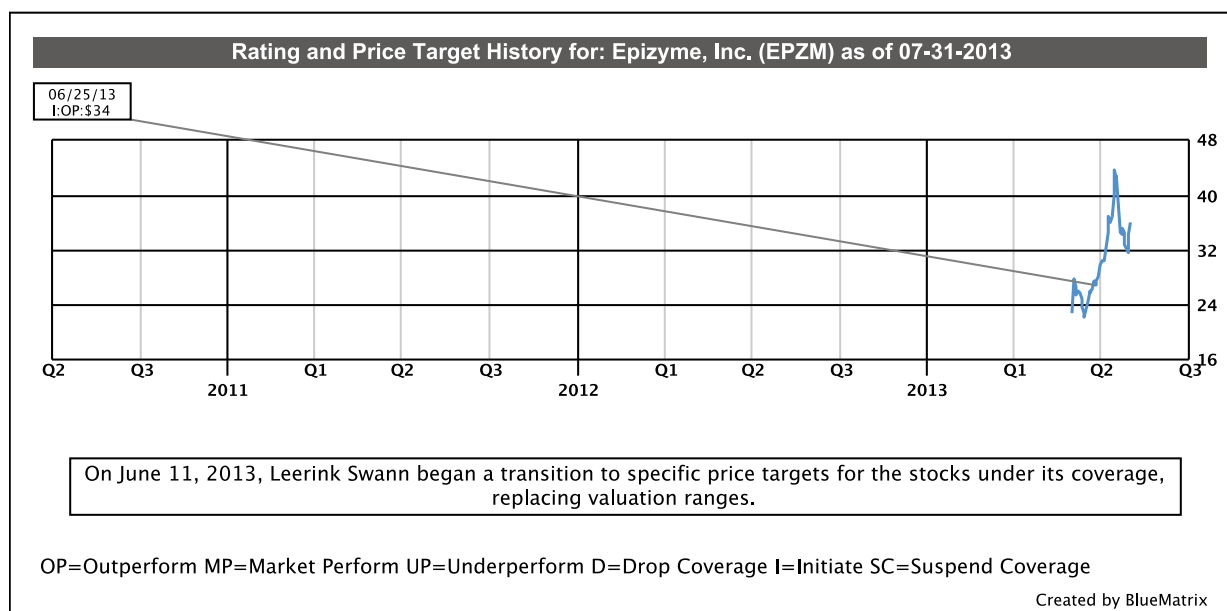
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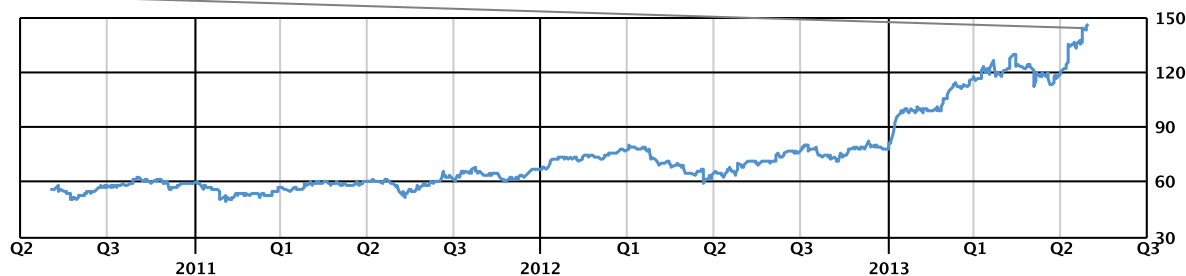
Commercial uptake may be limited by reimbursement, access or dosing concerns for EPZ-5676 and EPZ-6438.





### Rating and Price Target History for: Celgene, Inc. (CELG) as of 07-31-2013

07/26/13  
OP:\$165



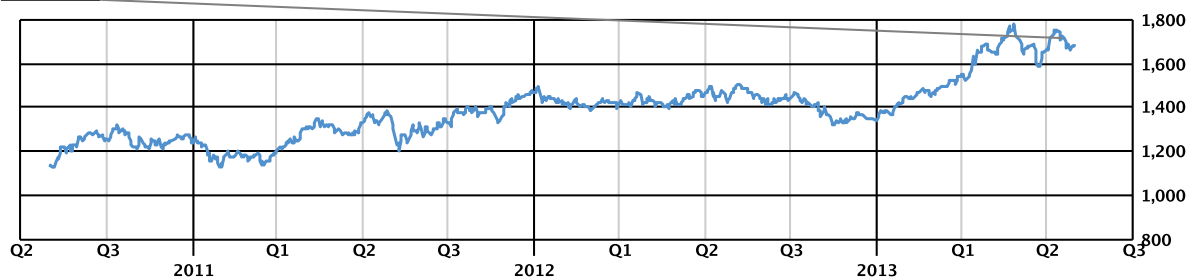
Leerink Swann initiated coverage of CELG with an Outperform rating on February 7, 2003. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

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

Created by BlueMatrix

### Rating and Price Target History for: GlaxoSmithKline plc (GSK LN) as of 07-31-2013

07/17/13  
MP:\$1830



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 06/30/13				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	103	62.80	30	29.00
HOLD [MP]	61	37.20	2	3.00
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

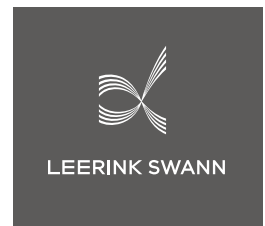
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Leerink Swann Consulting LLC, an affiliate of Leerink Swann LLC, is a provider of evidence-based strategy and consulting to the healthcare industry.

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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