Epizyme, Inc. (EPZM)

EPZ-5676 Phase I Data Suggest Higher Doses and Longer Duration of Therapy Required in MLL-r Disease

MARKET OUTPERFORM | Price: $18.78 | Target Price: $40.00

MARKET DATA

Price	$18.78
52-Week Range:	$18.60 - $45.72
Shares Out. (M):	28.4
Market Cap ($M):	$533.4
Average Daily Vol. (000):	131.0
Cash (M):	$140
Cash/Share:	$8.04
Enterprise Value (M):	$909
Float (M):	28.0
LT Debt (M):	$0

Cash (M): Reflects cash, equivalents, and short-term investments
Source: Thomson Reuters and JMP Securities LLC

FY DEC		2012A	2013E	2014E
Revenue ($M)	1Q	$5.7	$8.9A	$29.9
	2Q	--	$14.8A	$4.9
	3Q	--	$8.4A	$24.9
	4Q	--	$7.5	$38.7
	FY	**$45.2**	**$39.7**	**$98.5**
EPS	1Q	($3.38)	($4.24)A	$0.30
	2Q	--	($0.25)A	($0.41)
	3Q	--	($0.34)A	$0.26
	4Q	--	($0.50)	$0.58
	FY	**($0.72)**	**($1.99)**	**$0.94**

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

INVESTMENT HIGHLIGHTS

Initial Phase I results with DOTL1 inhibitor EPZ-5676 show good tolerability and preliminary evidence of clinical activity consistent with mechanism of action; reiterating Market Outperform rating on Epizyme with $40 price target based on NPV sum-of-the-parts and standardized CAGR valuation methodologies. Results from the first four dosing cohorts (12-54mg/m2 continuous infusion for 21 days of a 28-day cycle) show a clear proportional effect on drug exposure, as well as a dose- and time-dependent inhibition of the target histone methyl mark. Treatment effects, including reductions to circulating and bone marrow blasts and resolution of symptoms, were observed in four of eight treated patients with MLL-r. Enrollment of a fifth, 80mg/m2 cohort is ongoing, while a 20-patient expansion stage exclusively in MLL-r patients remains on schedule to begin by year end. Overall, these remain early days in assessing the clinical potential of '5676, as we suspect the treatment effects seen to date will translate into clinical response with further dose escalation.

Initial EPZ-5676 Phase I results show promise with remarkable tolerability and preliminary treatment effect, while leaving considerable headroom for improvement. While these data clearly satisfy the primary Phase I goal of establishing the drug's safety and tolerability, '5676's clinical activity is currently less definitive. As highlighted above and shown in detail in Figures 1 and 2, a range of surrogates of treatment effect were observed in four of the eight enrolled patients with MLL-r leukemia. That said, the paucity of response thus far (no remission or stable disease) and the absence of a clear positive dose/treatment effect relationship clearly has given investors pause. As evidenced by the effect on histone methyl mark inhibition over time (Figure 3), the pharmacodynamic effects of '5676 are quickly reversed during the seven-day treatment holiday, and could be attenuating the drug's treatment impact. By further dose escalation and a shift to a continuous infusion without the treatment holiday (28 days out of 28), EPZ-5676 has the potential to yield more rapid, potent and durable inhibition of the target methyl mark culminating in greater activity.

Well-tolerated safety profile enables higher doses and longer duration. To date, the company has not observed any dose-limiting toxicities or adverse events requiring dose interruption or reduction with '5676. One Grade 3, potentially treatment-related case of neutropenia was observed, but was non-treatment limiting. Another adverse event leading to discontinuation was not attributed to the drug. It is in light of this relatively benign safety profile that the company feels comfortable in pursuing a continuous infusion regimen, minus the seven-day drug holiday during the 20-patient expansion stage, with the potential to further dose escalate.

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Epizyme represents the rare opportunity to invest in a best-of-breed, pure-play, epigenetics-focused biotech company with clinical-stage assets and a robust drug discovery platform. We believe the company's clinical assets, EPZ-5676 and EPZ-6438, represent particularly compelling biology given that they are directed against clonally initiating mutations. This biologic focus, in combination with the selection of a genetically defined patient population, as providing capability for each asset to rapidly accelerate through the clinic and into registration-directed trials within 18 months. Combining these assets with a robust drug discovery product platform capable of consistently delivering multiple new therapeutic candidates targeting HMTs, and partnerships with GSK (Not Covered), Eisai, and Celgene (CELG, MO, $160 PT), we believe shares of EPZM will accrete significant additional value over the next six to twelve months as the potential for the company's pipeline comes into greater focus.

FIGURE 1. EPZ-5676 Dose Escalation MLL-r Patient Summary

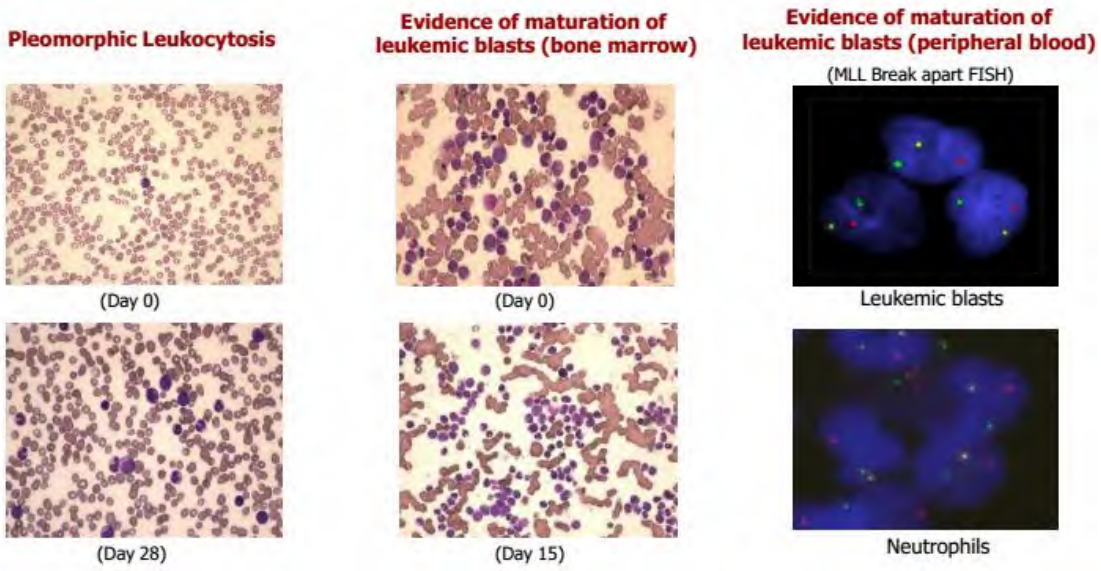
Cohort Dose	Dx	Treatment Effects	Cycles Completed
2 (24 mg/m2)	**ALL**	**90% circulating blast reduction (no bone marrow aspirate available) Resolution of fevers**	**Cycle 1+**
	AML	None observed	**Cycle 1+**
3 (36 mg/m2)	**AML**	**Maturation in blood and marrow (no change % marrow blasts) Leukocytosis 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 (2nd cycle)**
	AML	None observed	**Cycle 1+**
	CMML	*Too early to evaluate*	*On study (2nd cycle)*

*Maximum inhibition during treatment period

+Discontinuation due to disease progression

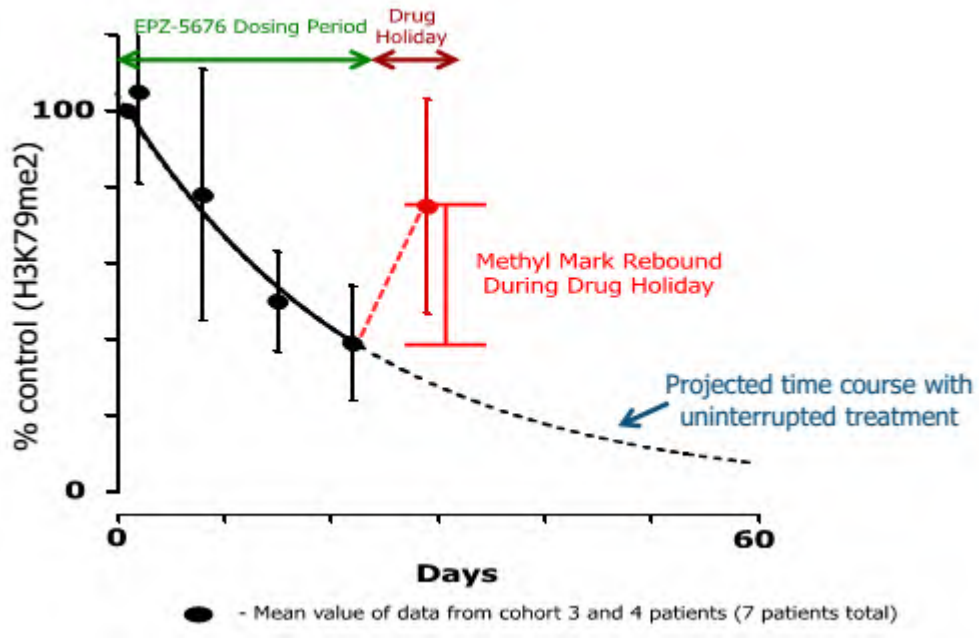
Source: Epizyme company presentation

FIGURE 2. EPZ-5676 Phase I Effects on Cell Differentiation



Source: JMP Securities LLC and Company Reports

FIGURE 3. EPZ-5676 Phase I Pharmacodynamics



Source: JMP Securities LLC and Company Reports

Company Description

Epizyme (EPZM) is a biopharmaceutical company, based in Cambridge, Massachusetts, focused on the discovery, development, and commercialization of personalized therapeutics for epigenetically-defined cancers. The company's technology is focused on the development of small molecule drugs specifically targeted against the individual members of the 96-member histone methyltransferase (HMT) class of enzymes. To date, the company has entered into strategic collaborations with Celgene, Eisai, and GSK regarding specific products, as well as the underlying technology platform.

Investment Risks

Clinical. Drug development is an inherently risky business. As clinical trials always carry a risk of failure, Epizyme's assets (EPZ-5676, EPZ-6438, or future products), may fail to demonstrate clinically meaningful levels of efficacy in ongoing or future trials. Further, it is unclear whether resistance pathways may develop to the epigenetic mechanisms being targeted.

Regulatory. The ability of Epizyme or its partners to market its drugs is dependent upon those drugs obtaining approval from the U.S. FDA and foreign regulatory authorities. Failure to achieve approval or delays in the timeline to approval could lead to substantial decrease in the company's share price.

Competitive. Epigenetics is an increasingly competitive field and Epizyme will face competition both from companies focused in the space, as well as players targeting related mechanisms. As such, there is no assurance that Epizyme's product will be competitive or differentiated from other drugs.

Commercialization. Epizyme has stated its plans to retain U.S. commercial rights to its products and develop a commercial infrastructure to market those products. The company has limited commercial experience and infrastructure in place. As such, the company will face significant expenses developing or acquiring these resources.

Reimbursement. There is no guarantee that Epizyme, or its partners, will garner adequate reimbursement for its products. Failure to obtain adequate levels of reimbursement could negatively impact the company's share price.

Partners. Epizyme has formed development and commercial partnerships with Celgene, Eisai, and GSK. Epizyme is highly dependent upon these partnerships to provide non-dilutive sources of capital. Celgene and Eisai are critical to the development and commercialization of Epizyme's clinical stage assets. Changes to or terminations of these partnerships could affect Epizyme's shares negatively.

Financial. Post-IPO, we estimate that the company will end 2Q13 with approximately $160MM in cash and cash equivalents. While the company has guided that even excluding any milestones payments from Celgene, Eisai, or GSK (which we expect) it has adequate resources to fund the company into 2015, we wholly expect the company to revisit the capital markets to further fund clinical development of its assets, develop a commercial infrastructure in the U.S., and to identify other assets using its platform technology and expertise. We currently forecast that the company will conduct secondary offerings in 2014 and 2015 before reaching profitability in 2017. While we view this as common for similar stage biotechnology companies, the risk of dilution may create an overhang at times.

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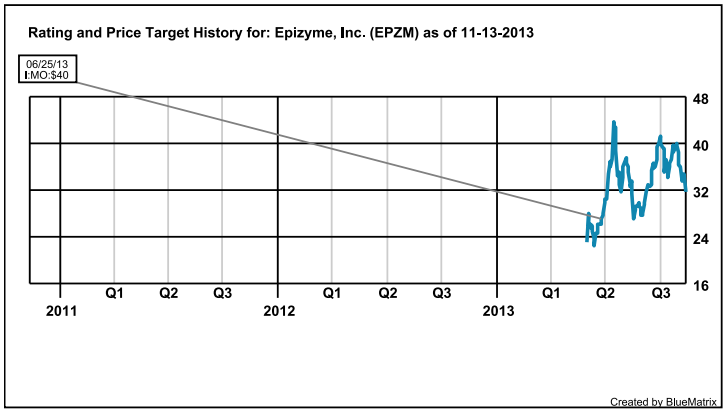
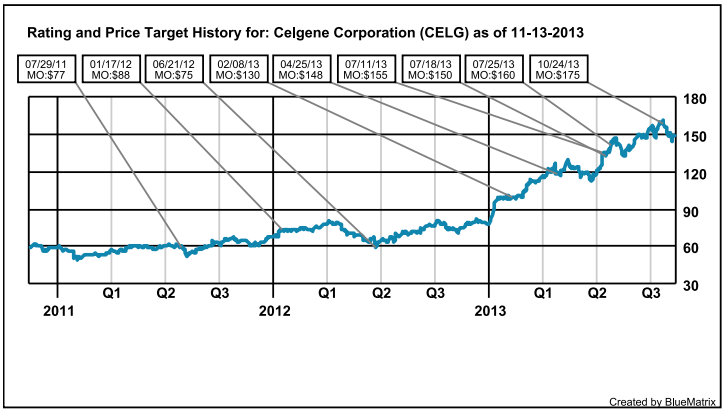
MARKET OUTPERFORM	Buy	249	*61.18%*	Buy	249	*61.18%*	81	*32.53%*
MARKET PERFORM	Hold	152	*37.35%*	Hold	152	*37.35%*	24	*15.79%*
MARKET UNDERPERFORM	Sell	6	*1.47%*	Sell	6	*1.47%*	0	*0%*
TOTAL:		407	*100%*		407	*100%*	105	*25.80%*

Stock Price Chart of Rating and Target Price Changes:

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.





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