Epizyme, Inc. (EPZM)

Focus Centered on Qualification of '5676 Activity Heading into ASH

MARKET OUTPERFORM | Price: $20.81 | Target Price: $40.00

MARKET DATA

Price	$20.81
52-Week Range:	$18.10 - $45.72
Shares Out. (M):	28.4
Market Cap ($M):	$591.0
Average Daily Vol. (000):	46.0
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

Upcoming ASH event offers opportunity for clarity regarding preliminary treatment effects seen with EPZ-5676 and the high unmet need in MLL-rearranged leukemia; reiterate our Market Outperform rating on Epizyme and our $40 price target. Epizyme will host an R&D event in conjunction with the 55th ASH Annual Meeting on Monday, December 9, wherein invited physician investigators, including Martin S. Tallman of Memorial Sloan-Kettering, are expected to provide further color regarding the recently disclosed Phase I data with DOT1L inhibitor EPZ-5676 in patients with mixed lineage leukemia (MLL-r). In our view, further characterization of the treatment effects described thus far and their predictive significance in the ongoing dose escalation and expansion cohort Phase I trial have the potential to alleviate some of the negative sentiment saddling EPZM in the weeks following the Phase I data release November 14. In addition, a detailed review of pathogenesis and treatment paradigm in synovial sarcoma by Charles Roberts of the Dana-Farber Cancer Institute is expected to yield further insight into the opportunities and clinical prospects with EZH2 inhibitor EPZ-6438 in solid tumors. We derive our $40 price target through a combination of NPV sum-of-the-parts and standardized CAGR valuation methodologies.

The Street underappreciates the significance of treatment effects seen to date with '5676, in our view. As reviewed previously in our 11/14 note and shown in Figures 1 and 2, results from the dose escalation Phase I study thus far have been a range of surrogate treatment effects, including reductions to circulating blast counts, bone marrow blast cell differentiation, and resolution of symptoms, including leukocytosis (abnormally high white blood cell count and leukemia cutis (skin lesions due to infiltrating leukocytes). While complete remission remains the benchmark for establishing '5676 clinical activity, we believe the effects seen to date are positive indicators, connecting the dots to meaningful activity with higher doses and longer duration on therapy. Expert and '5676-specific anecdotal commentary by the physician panel should help contextualize Phase I results within the current prognosis for MLL-r patients and better define clinical significance.

Current dosing cohort of 80mg/m2 may offer near-term opportunity reassess activity. A fifth dose cohort of 80mg/m2 (21 out 28 days continuous infusion) is currently enrolling patients, with a 20-patient expansion cohort evaluating a starting dose of 80mg/m2 without the drug holiday exclusively in patients with MLL-r slated to begin by year-end. While the company has not set expectations for further Phase I updates in 2013, we suspect the current dosing cohort may achieve the requisite proximal and sustained H3K79 methyl inhibition to effect responses, offering a meaningful near-term opportunity to reassess activity of '5676, particularly if the trial is amended to allow for 28-day continuous infusion through petitioning the IRB.

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With expectations as low as they are, we spot appreciable upside from incremental clarity around EPZ-5676 heading into ASH. Much in the way ARIA (MP) has seen acute gains (+77% since November 21) in reaction to the formal CHMP decision to keep Iclusig EU marketing approval largely intact, we suspect relatively incremental data could have an outsized impact on EPZM near-term. Longer-term, we continue to view EPZM as a rare opportunity to invest in a best-of-breed, pure play in the epigenetics space, offering both clinical-stage assets and a robust drug discovery platform.

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

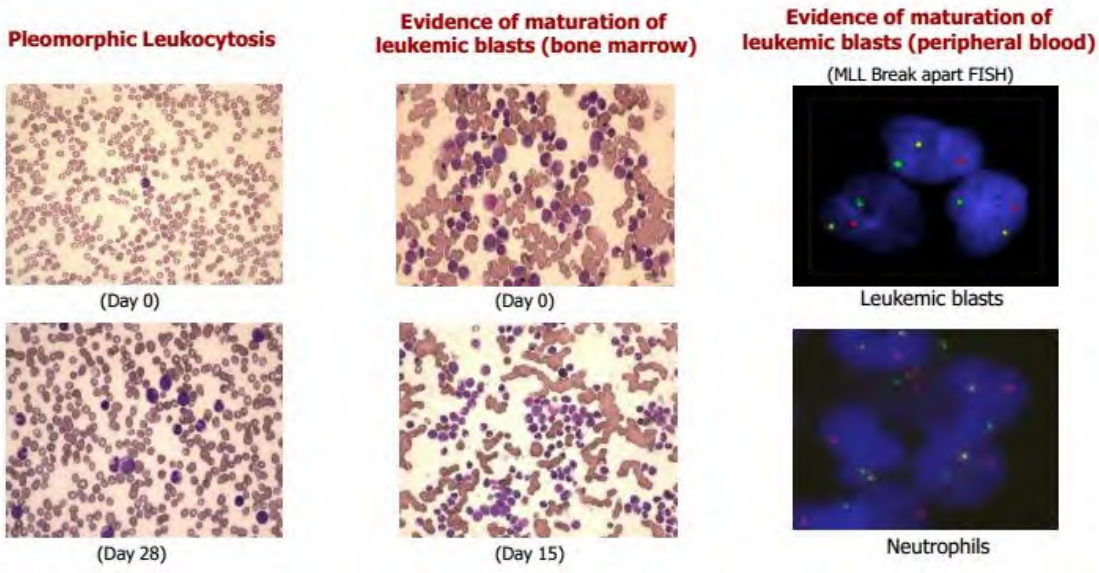
Cohort Dose	Dx	Treatment Effects	Cycles Completed
2 (24 mg/m2)	**ALL**	**90% circulating blast reduction (no bone marrow aspirate available) Resolution of fevers**	**Cycle 1⁺**
	AML	None observed	**Cycle 1⁺**
3 (36 mg/m2)	**AML**	**Maturation in blood and marrow (no change % marrow blasts) Leukocytosis 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: Epizyme company presentation

FIGURE 3. Upcoming Milestones

Timing	Drug	Milestones
4Q13	EPZ-5676	MLL-r Phase 1 expansion cohort initiation, data in 2014
1H14	EPZ-6438	Initiation of Phase 2 expansion cohort enrollment in EZH2+ NHL
2014	EPZ-5676	MLL-r pediatric Phase 1 expected in 2014
2014	EPZ-5676	MLL-PTD Phase 2 expansion cohort expected
2014	EPZ-6438	NHL Phase 1 dose escalation data
2014	EPZ-6438	NHL Phase 2 expansion cohort expected initiation
2014	EPZ-6438	Synovial sarcoma Phase 2 expected initiation

Source: Epizyme company presentation

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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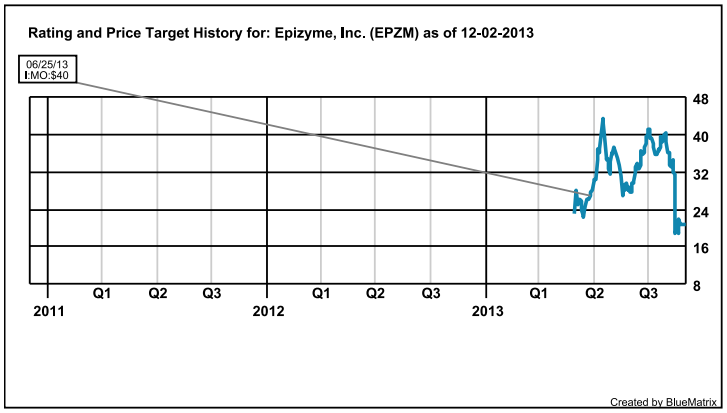
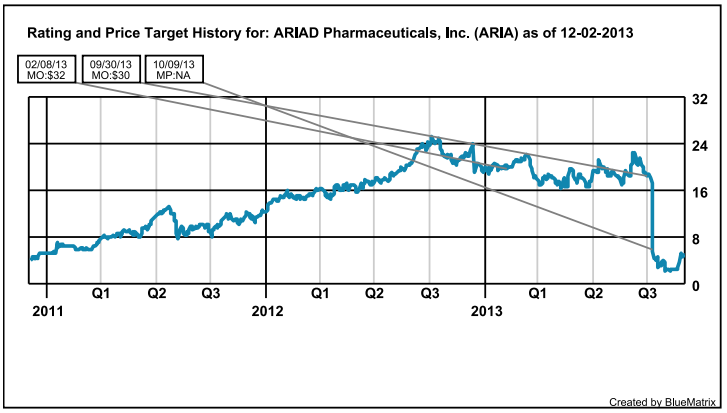
MARKET OUTPERFORM	Buy	235	*56.76%*	Buy	235	*56.76%*	87	*37.02%*
MARKET PERFORM	Hold	137	*33.09%*	Hold	137	*33.09%*	24	*17.52%*
MARKET UNDERPERFORM	Sell	5	*1.21%*	Sell	5	*1.21%*	0	*0%*
COVERAGE IN TRANSITION		37	*8.94%*		37	*8.94%*	0	*0%*
TOTAL:		414	*100%*		414	*100%*	111	*26.81%*

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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