Calithera Biosciences, Inc. (CALA)

Three Presentations Bolster Confidence in CALA's Glutaminase Inhibitor Program

MARKET DATA

Price	$13.66
52-Week Range:	$6.51 - $33.48
Shares Out. (M):	17.6
Market Cap ($M):	$240.4
Average Daily Vol. (000):	545.0
Cash (M):	$102
Cash/Share:	$5.69
Enterprise Value (M):	$343
Float (M):	17.8
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2014A	2015E	2016E
Revenue ($M)	1Q	NA	$0.0	--
	2Q	$0.0	$0.0	--
	3Q	$0.0	$0.0	--
	4Q	$0.0	$0.0	--
	FY	**$0.0**	**$0.0**	**$0.0**
EPS	1Q	--	($0.39)	--
	2Q	($1.22)	($0.42)	--
	3Q	($0.29)	($0.43)	--
	4Q	($0.37)	($0.44)	--
	FY	**($1.47)**	**($1.69)**	**($3.29)**
	P/E	NM	NM	NM

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

MARKET OUTPERFORM | Price: $13.66 | Target Price: $20.00

INVESTMENT HIGHLIGHTS

Three Calithera Biosciences presentations yield confidence in the company's glutaminase inhibitor program; reiterate our Market Outperform rating and $20 price target based on a synthesis of discounted cash flow, sum-of-the-parts and CAGR valuation methodologies. Yesterday, we attended three CALA presentations (two oral and one poster) at the American Association for Cancer Research Annual Meeting 2015 being held in Philadelphia, highlighting preclinical work with the company's lead asset, CB-839, and shedding light on the potential for future directions for this agent. These presentations gave us further confidence in CALA's glutaminase inhibitor program and in CB-839 specifically, which is currently in the clinic for solid and hematological malignancies (Figure 1). We look forward to additional data readouts from the CB-839 program at ASCO 2015 in Chicago, May 29-June 2.

Possible biomarker to predict drug sensitivity. In a poster presentation of preclinical studies undertaken at Columbia University Medical Center using sarcoma cell lines, the key takeaway was that specific cell lines were glutamine dependent and those cells were correspondingly sensitive to CB-839 treatment. In entirely separate studies, mirroring the notion of glutamine dependency of specific carcinomas, the glutamine dependency of non-small cell lung cancer cells (NSCLC) to CB-839 was interrogated by Boroughs et al. from the University of Texas. Taking this notion one step further, the investigators sought to identify biomarkers to predict the sensitivity of NSCLC cells to the drug. After analyzing 81 cell lines, ~40 were found to be sensitive to CB-839, which also correlated strongly with glutamine dependence and glutamine secretion (Figures 2 & 3). Although no clear relationships were found between the mutational status of the cell lines and sensitivity to CB-839, the group found that NSCLC cell lines carrying KRAS mutations did correlate with sensitivity to the drug (Figure 4). Interestingly, expression of Phospho-Rb (S807/811) (Figure 5) and Smad3 also appeared to correlate with drug sensitivity. Rb (retinoblastoma gene product) is a protein required for the cell to transit from the G1 to S progression of the cell division cycle. Generally maintained in the hypophosphorylated state, this protein is unable to restrict progression of the cell cycle when it becomes hyperphosphorylated. The study by Boroughs et al. suggests that these lines sensitive to the drug may have higher signals to replicate, and glutaminase (enzyme that converts glutamine to glutamate) inhibition may in effect cause replication stress. Thus, the ratio of hyperphosphorylated to hypophosphorylated Rb protein may serve as a potential biomarker for tumors sensitive to CB-839, although further work is necessary to validate this hypothesis.

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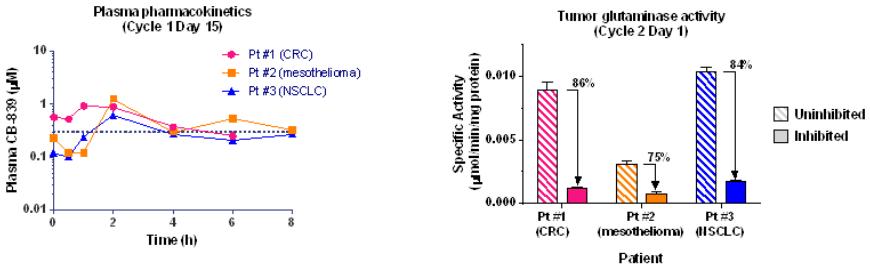
Synergies with kinase inhibitors. Another oral presentation we attended yesterday was "CB-839, a selective glutaminase inhibitor synergizes with signal transduction pathway inhibitors to enhance anti-tumor activity" presented by Dr. Francesco Parlati, Director of Biology at Calithera Biosciences. As a reminder, CB-839, which impacts multiple metabolic pathways, has been shown to exhibit anti-tumor activity in several preclinical models, including in triple negative breast cancer (TNBC) by causing a decrease in mTOR1 signaling. In this study, Rodriguez et al. reviewed combinations of CALA's lead asset with several agents with varying mechanisms in multiple cancer cell lines. As with the abovementioned studies, the cancer cell lines analyzed were also first shown to be sensitive to glutaminase inhibition (Figure 6), providing further support for CALA's program. When combined with GlaxoSmithKline's (GSK, NC) pan receptor tyrosine kinase inhibitor Votrient (pazopanib) as well as Novartis' (NVS, NC) mTOR inhibitor Afinitor (everolimus; Figure 7) in renal cell carcinoma (RCC) cell lines, CB-839 exhibited synergy (combination index, CI: 0.09-0.085 and 0.48-0.54 respectively). When CB-839 was examined in combination with Genentech's (NC) Tarceva (erlotinib) in several non-small cell lung cancer lines (NSCLC), synergy was seen in this setting as well (CI: 0.39-0.75). Data were presented demonstrating that NSCLC cell lines carrying EGFR or KRAS mutations have enhanced sensitivity to the CALA drug (Figure 8). Further, in a KRAS mutant NSCLC line H2122, CB-839 showed an effect with a MEK inhibitor drug in development by AstraZeneca (AZN, NC), selumetinib (CI: 0.46) (Figure 8); additionally, anti-tumor activity was observed in an *in vivo* H2122 NSCLC xenograft model. However, in the KRAS wild type cell line H661, the synergy was weak (CI: 0.9), which may suggest other mechanisms apart from gaining enrichment from glutamine may be at play; and therefore depleting glutamine sources may be insufficient to produce a synergistic effect. Taken together, if the data hold, we anticipate that CALA will pursue drug combination studies in NSCLC and/or RCC patients with the above agents in the near future.

We remain bullish on CALA and we see recent weakness as overdone. Calithera is an early-stage, oncology-focused drug discovery and development company attempting to exploit the increasing knowledge of the cancer cell's ability to hijack the energy production mechanisms required for the utilization of energy from a variety of sources. The company's first product candidate, CB-839, is a novel inhibitor of glutaminase, an enzyme that converts glutamine to glutamate, the latter of which is a critical feedstock for the cell's energy production system. The company was founded by Susan Molineaux, founder of Proteolix, the company that developed Kyprolis (carfilzomib) and which was eventually sold to Onyx for $700MM. Onyx, in turn, was sold to Amgen (AMGN, NC) in 2013 for $10 billion.

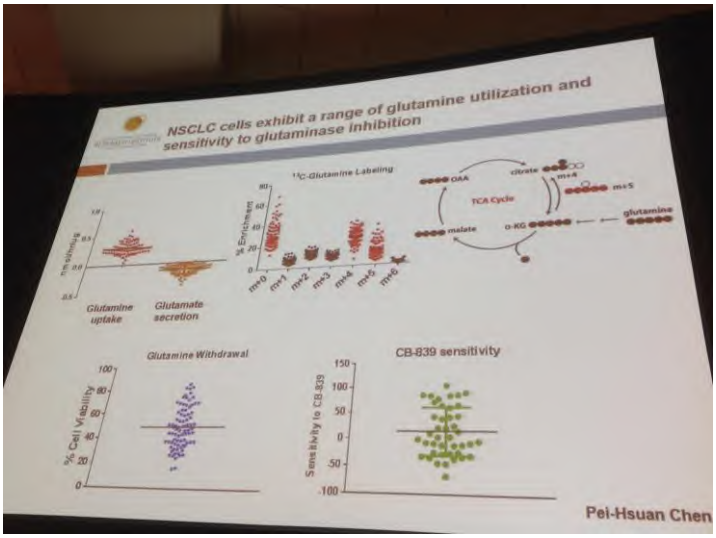
FIGURE 1. Pharmacodynamic Effects of CB-839

Patients (Early cohorts)	Tumor Type	Glutaminase Inhibition in Tumor 4 h post-dose
1	Colon (CRC)	86%
2	Mesothelioma	75%
3	Non Small Cell Lung (NSCLC)	84%



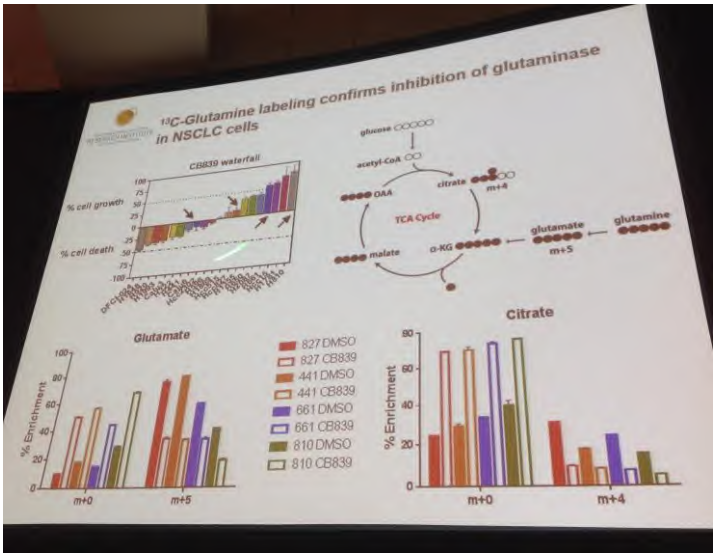
Source: Company Presentations

FIGURE 2. Glutamine Utilization and Sensitivity to Glutaminase Inhibition



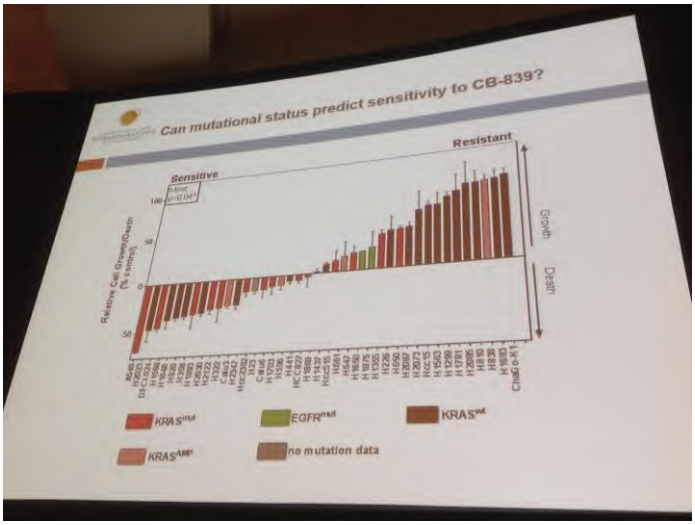
Source: Company Presentations

FIGURE 3. Inhibition of Glutaminase in NSCLC Cells



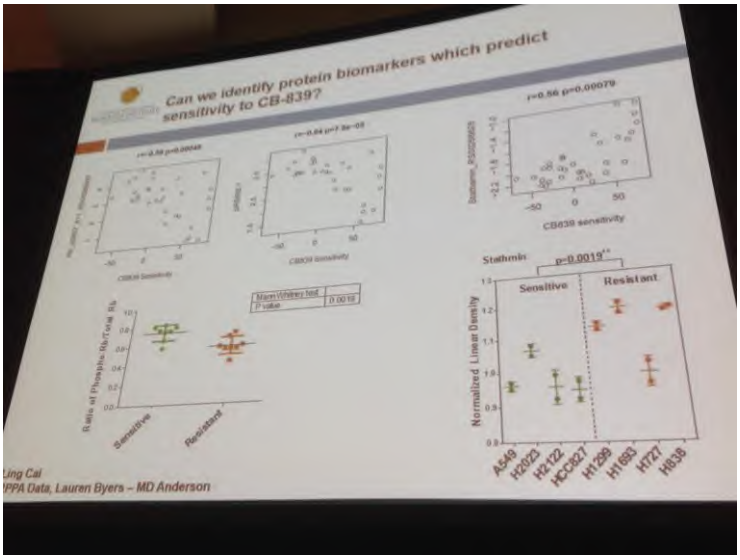
Source: Company Presentations

FIGURE 4. Correlating Mutational Status with Drug Sensitivity



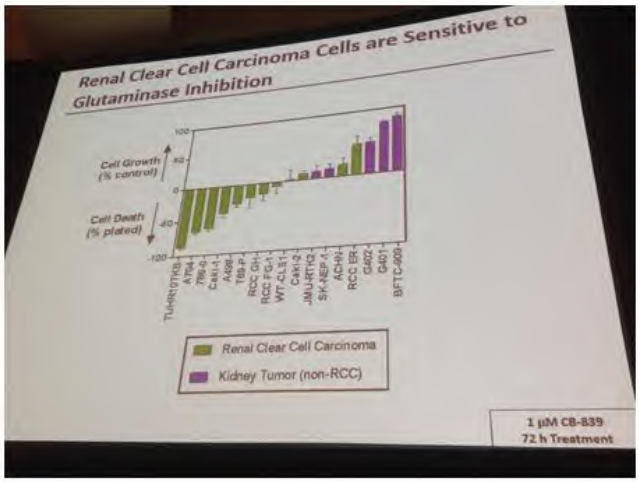
Source: Company Presentations

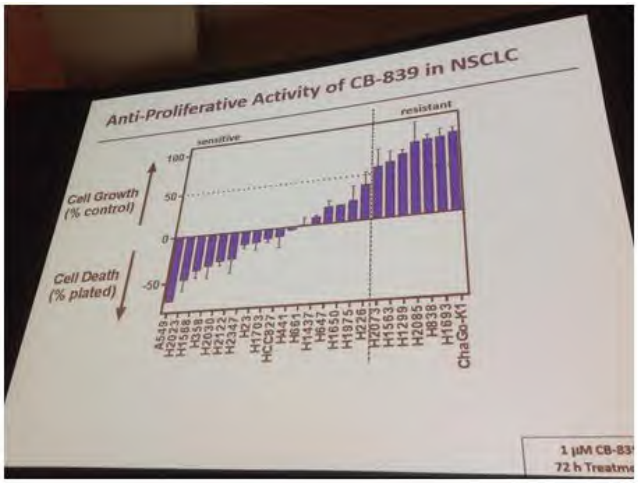
FIGURE 5. Potential Biomarker to Predict CB-839 Selectivity



Source: Company Presentations

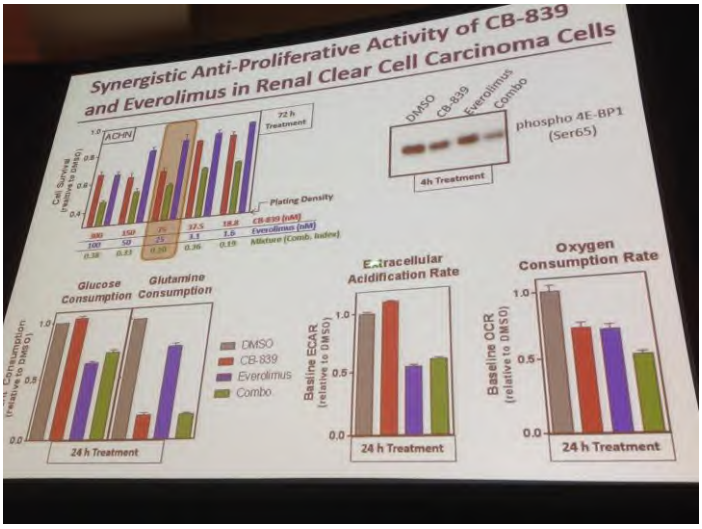
FIGURE 6. RCC and NSCLC Cells are Sensitive to CB-839





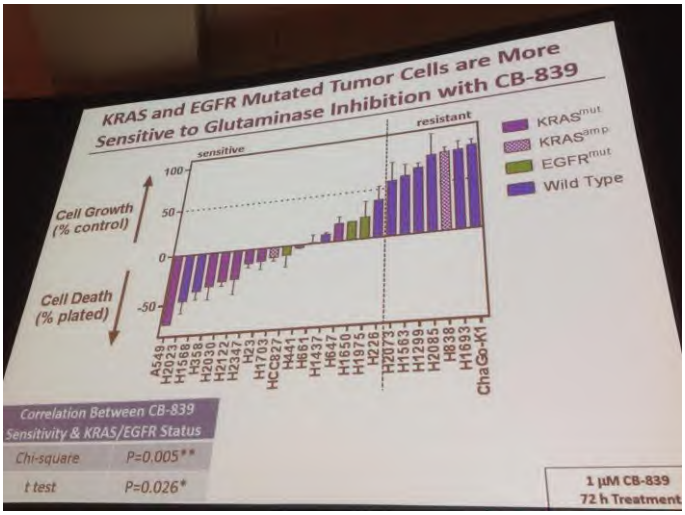
Source: Company Presentations

FIGURE 7. Synergy of CB-839 with Everolimus in RCC cells



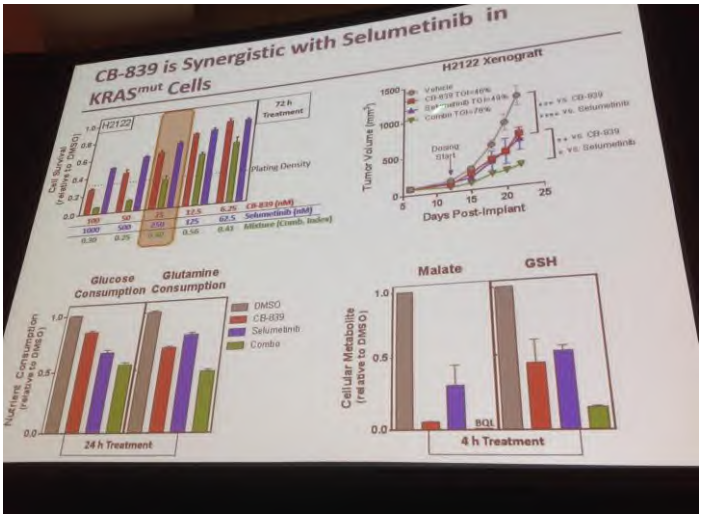
Source: Company Presentations

FIGURE 8. KRAS and EGFR Mutated Tumor Cells are More Sensitive to CB-839



Source: Company Presentations

FIGURE 9. Synergy with Selumetinib in KRAS Mutant Cells



Source: Company Presentations

FIGURE 10. CALA Income Statement

Income Statement ($MM)	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Product Sales and Royalties:															
CB-839															
US Sales					-	-	-	54.6	310.5	625.0	965.1	1,268.5	1,459.7	1,551.8	1,616.9
ROW Royalties					-	-	-	-	6.3	41.1	86.6	132.9	182.8	211.1	226.2
Total Product Sales and Royalties	-	-	-	-	-	-	-	54.6	316.8	666.1	1,051.7	1,401.4	1,642.5	1,762.9	1,843.1
Cost of Goods Sold						-	-	6.5	37.3	75.0	115.8	152.2	175.2	186.2	194.0
Gross Profit	-	-	-	-	-	-	-	48.0	279.5	591.1	935.9	1,249.2	1,467.3	1,576.7	1,649.1
Operating Expenses:															
Research and development	5.7	6.5	7.3	8.0	27.5	55.0	110.0	170.5	221.7	266.0	292.6	321.8	354.0	389.4	428.4
% Growth					*66.9%*	*100.0%*	*100.0%*	*55.0%*	*30.0%*	*20.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*
% Total US Net Sales								*312%*	*71%*	*43%*	*30%*	*25%*	*24%*	*25%*	*26%*
General and administrative	2.0	2.2	2.3	2.4	8.9	19.6	58.7	105.7	153.3	191.6	210.8	229.8	248.2	260.6	273.6
Total operating expenses	7.7	8.7	9.6	10.4	36.4	74.6	168.7	276.2	375.0	457.6	503.4	551.6	602.2	650.0	702.0
Operating income (loss)	(7.7)	(8.7)	(9.6)	(10.4)	(36.4)	(74.6)	(168.7)	(228.2)	(95.4)	133.5	432.5	697.6	865.2	926.7	947.2
Operating margin (%)								*-418.1%*	*-30.1%*	*20.0%*	*41.1%*	*49.8%*	*52.7%*	*52.6%*	*51.4%*
Interest income															
Interest expense															
Total other income, net	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pretax income (loss)	(7.7)	(8.7)	(9.6)	(10.4)	(36.4)	(74.6)	(168.7)	(228.2)	(95.4)	133.5	432.5	697.6	865.2	926.7	947.2
Income tax benefit (provision)					0.0	0.0	0.0	0.0	4.8	(13.3)	(86.5)	(209.3)	(302.8)	(324.3)	(331.5)
Tax Rate									*5%*	*10%*	*20%*	*30%*	*35%*	*35%*	*35%*
Comprehensive income (loss)	(7.7)	(8.7)	(9.6)	(10.4)	(36.4)	(74.6)	(168.7)	(228.2)	(90.7)	120.1	346.0	488.3	562.3	602.4	615.7
Basic EPS to common shareholders	$ (0.39)	$ (0.42)	$ (0.43)	$ (0.44)	**$ (1.69)**	**$ (3.29)**	**$ (6.07)**	**$ (6.88)**	**$ (2.60)**	**$ 3.28**	**$ 9.01**	**$ 12.10**	**$ 13.28**	**$ 13.54**	**$ 13.18**
Diluted EPS to common shareholders	$ (0.39)	$ (0.42)	$ (0.43)	$ (0.44)	**$ (1.69)**	**$ (3.29)**	**$ (6.07)**	**$ (6.88)**	**$ (2.60)**	**$ 3.28**	**$ 9.01**	**$ 12.10**	**$ 13.28**	**$ 13.54**	**$ 13.18**
Basic shares outstanding	19.7	20.9	22.2	23.5	21.6	22.7	27.8	33.2	34.8	36.6	38.4	40.3	42.4	44.5	46.7
Diluted shares outstanding	19.7	20.9	22.2	23.5	21.6	22.7	27.8	33.2	34.8	36.6	38.4	40.3	42.4	44.5	46.7

Source: JMP Securities LLC and Company Reports

Company Description

Calithera Biosciences, based in San Francisco, CA, is a clinical-stage biotechnology company focused on the discovery and development of novel small molecules directed against cancer and immune cell metabolism to treat both solid tumor and hematologic malignancies. The company's lead product candidate, CB-839, is an internally discovered and wholly owned potent, oral selective inhibitor of glutaminase. Inhibition of glutaminase by CB-839, in effect, starves cancer cells of glutamate - a critical substrate for cancer cell metabolism, growth, and survival. CB-839 is currently in Phase I analysis in both solid and hematologic tumors. Planned Phase Ib cohorts in combination with standard of care agents in triple negative breast cancer and multiple myeloma are expected to be initiated. A second wholly owned pre-clinical candidate is Calithera's first-in-class arginase inhibitor, directed at immune checkpoint modulation and engaging the activation of cytotoxic T-cells. Calithera intends to submit an IND to the FDA for the arginase program in late 2015.

Investment Risks

Potential risks to our price target include, but are not limited to, clinical, regulatory, commercial, and competitive factors.

Scientific and clinical. Drug development is an inherently risky business. Cancer metabolism, and specifically, the role of glutaminase in cancer pathogenesis, remains largely unproven, creating significant risk associated with Calithera's scientific platform. Like all clinical trials, CB-839 clinical development carries some risk of failure. CB-839 may fail to maintain the requisite safety or to demonstrate meaningful efficacy to warrant further development through to regulatory approval.

Regulatory and commercial. The ability of Calithera or its potential partners to market its drugs depends on those drugs obtaining approval from the FDA and foreign regulatory agencies. Failure to achieve approval or delays in the timelines to approval could negatively impact the company's share price.

Competitive. Oncology drug development is an increasingly competitive field. Calithera faces competition from companies developing small molecule therapies also directed at cancer cell metabolism in ways that may resemble those of Calithera's pipeline. Small molecule oncology therapies employing other mechanisms of action are also in development by several biopharma companies to treat similar patient populations to that of CB-839 and may yield superior risk-benefit outcomes. Some of these companies may have access to greater resources, development, and commercial expertise compared to Calithera.

Financial. We anticipate that Calithera may seek additional equity financing in the form of a secondary offering in order to complete the development of CB-838 and advance its future pipeline candidates, exposing existing shareholders to some degree of dilution risk.

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Market Outperform (MO): JMP Securities expects the stock price to outperform relevant market indices over the next 12 months.
Market Perform (MP): JMP Securities expects the stock price to perform in line with relevant market indices over the next 12 months.
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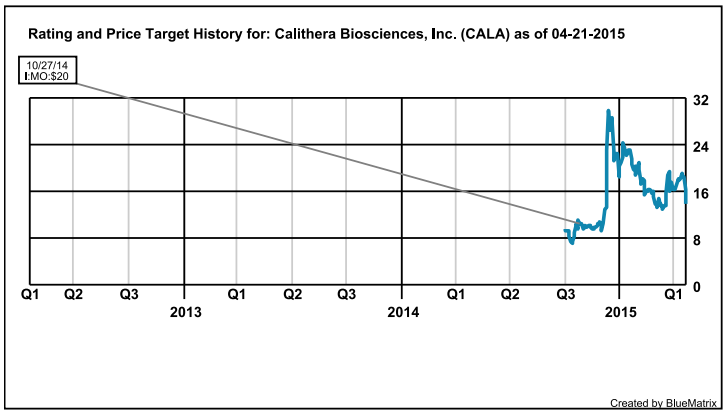
JMP Rating	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	# Co's Receiving IB Services in Past 12 Months	*% of Co's With This Rating*
MARKET OUTPERFORM	Buy	287	*63.36%*	Buy	287	*63.36%*	97	*33.80%*
MARKET PERFORM	Hold	145	*32.01%*	Hold	145	*32.01%*	20	*13.79%*
MARKET UNDERPERFORM	Sell	8	*1.77%*	Sell	8	*1.77%*	0	*0%*
COVERAGE IN TRANSITION		12	*2.65%*		12	*2.65%*	1	*8.33%*
TOTAL:		453	*100%*		453	*100%*	118	*26.05%*

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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