Calithera Biosciences, Inc. (CALA)

CALA Debuts First-in-Human Data with CB-839 at ASCO

MARKET DATA

Price	$10.47
52-Week Range:	$6.51 - $33.48
Shares Out. (M):	17.6
Market Cap ($M):	$184.3
Average Daily Vol. (000):	149.0
Cash (M):	$94
Cash/Share:	$5.25
Enterprise Value (M):	$141
Float (M):	17.8
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2014A	2015E	2016E
Revenue ($M)	1Q	$0.0	$0.0A	--
	2Q	$0.0	$0.0	--
	3Q	$0.0	$0.0	--
	4Q	$0.0	$0.0	--
	FY	**$0.0**	**$0.0**	**$0.0**
EPS	1Q	--	($0.40)	--
	2Q	($1.22)	($0.42)	--
	3Q	($0.29)	($0.43)	--
	4Q	($0.37)	($0.44)	--
	FY	**($1.47)**	**($1.69)**	**($3.31)**
	P/E	NM	NM	NM

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

MARKET OUTPERFORM | Price: $10.47 | Target Price: $20.00

INVESTMENT HIGHLIGHTS

ASCO marks the introduction of encouraging initial clinical data with CB-839; reiterate our Market Outperform rating and $20 price target for Calithera Biosciences based on a synthesis of DCF, SOTP, and comparable valuation methodologies. We are currently attending American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago where Dr. James J. Harding presented initial clinical results of one of the three ongoing Phase I trials with CB-839, a first-in-class oral glutaminase inhibitor. As a reminder, CALA has initiated three open-label, Phase I studies in 2014 with its lead agent, CB-839 (currently in the dose expansion phase with an RP2D of 600mg BID with food) in three tumor types: select solid tumors, multiple myeloma and acute myeloid leukemias. The data in solid tumors were also highlighted and reviewed in a poster discussion session by Dr. Robert Wesolowski entitled, *Exploiting Metabolic Processes as Therapeutic Targets*, and elaborated upon further at CALA's ASCO Analyst Meeting. Taken together, these presentations describing the initial clinical safety and tolerability data, including early signs of biologic activity with the drug as a monotherapy, have further bolstered our view of the clinical program.

CB-839 demonstrating single-agent clinical activity. Recall that the Phase I study is looking at safety, tolerability, and the recommended Phase II dose (RP2D) of CB-839 in patients that have had a median of three prior therapies for metastatic solid tumors. Of note, one subcohort included patients that were genetically identified to carry mutations in three enzymes (IDH, SDH, and FH) in the TCA cycle, which are dependent on glutamine and work downstream of glutaminase. The full study has multiple arms, with an initial standard 3+3 dose escalation Phase I (Figure 2). The expansion cohorts with various malignancies of interest are expected to enroll to either monotherapy or in combination with other therapies, as an RP2D has now been established. As of April 15, 59 patients were evaluable for safety and 48 for efficacy: 32 patients on a three times daily schedule (100-800 mg TID) and 27 patients on twice daily fed schedule (600 or 800 mg BID) (Figure 3).

In the dose-escalation portion of the trial that is now complete, a maximum tolerated dose (MTD) had not been reached at doses up to 800 mg TID. However, radiographic stable disease (SD) was observed in 19% (6/31 response-evaluable patients) on the dose-escalation study at the TID schedule and a remarkable 41% (7/17 response-evaluable patients) on the BID schedule with a variety of solid tumors. These included two triple negative breast cancer (TNBC) patients and one renal cell carcinoma (RCC) patient who had SD for 323, 218 and 240 days, respectively, and remain on study. Given that these patients have received regimens prior to CB-839, Dr. Wesolowski, in his review of the poster, found the SD data in the BID cohort particularly noteworthy. In our view, the results bode well for the program given that patients were also presumably

Michael G. King, Jr.
mking@jmpsecurities.com
(212) 906-3520

treated at sub-therapeutic levels in the dose-ascending study, including one TNBC patient that reached SD (250 mg TID; Figure 3).

Manageable adverse events observed. As of May 15, a total of 76 patients have been enrolled in the solid tumor study with two discontinuations (2/59) due to an adverse event and eight (8/59) that may have been attributable to Grade 3 or 4 adverse events. Although one dose limiting toxicity was observed at 250 mg TID, where a Grade 3 increase in creatinine levels occurred in a patient with diabetes, none have been observed since, according to management. Additionally, the rates of adverse events are likely in line with patients with advanced disease, given the heavily pretreated population. Although 13.6% patients experienced Grade 3 or 4 adverse events (primarily elevations in AST and ALT), these events were transient and were rapidly reversible upon treatment interruption. Importantly, Dr. Wesolowski also noted in his discussion that patients who received a twice daily schedule (a schedule to be followed in the next phase of the trials) exhibited much less instances of AST and ALT elevations. Indeed, only one patient developed a Grade 3 ALT at the twice daily dosing schedule.

Of significance, other side effects observed, which were of mild or moderate intensity, could be reduced with a BID fed schedule. Although BID fed schedule may prove to be an acceptable dosing regimen for patients as a monotherapy, we note that in the planned combination studies (Figure 4)—at least where the second agent may induce AEs such as nausea and vomiting —compliance may prove to be difficult in such a setting. Even so, a half-life of four hours enabled treatment with CB-839 to be moved to a BID fed schedule, which coincidentally also demonstrates less PK variability when compared with the TID schedule (Figure 5). Overall it appears CB-839 has acceptable PK/PD characteristics as the drug appears to have minimal maximum exposure of the study drug in the plasma of patients (Figure 6). Further, patients who received 600 mg BID, appeared to have minimum concentrations that was above 200 ng/mL (the level at which 90% or greater glutaminase inhibition is expected with peripheral blood platelets) (Figure 7). When tumor samples were evaluated at Day 1 of Cycle 2, the reduction of glutaminase activity is observed in various tumor samples (Figure 7). Thus, although the BID fed cohort is still immature, we find the data compelling.

New AML data unveiled at Analyst Event. As a reminder, CALA will present updated data from the dose-escalation portion of the Phase 1 trial in acute myeloid leukemia (AML) patients at the 20th Congress of the European Hematology Association (EHA) to be held on June 11-14 in Vienna. Briefly, oral CB-839 was administered at doses ranging from 100 mg to 1000mg to R/R AML patients (over the age of 65 and ineligible for high dose therapy), continuously in 21-treatment cycles. At the time of the abstract cut off, data on 15 evaluable patients were included. As of April 15, CALA has enrolled 18 leukemia patients in the study (16 patients on TID schedule and 2 on BID schedule) (Figure 8). The TID arm also included one patient with an IDH1 mutation and two patients carrying the IDH2 mutation. Enrollment had initially reached 19. However, the 19th patient discontinued treatment as a result of CNS-related complications arising from AML directly. Importantly, despite progression in the CNS, the patient achieved a CR in the bone marrow with incomplete recovery of peripheral counts after 6 cycles of dosing. There were no discontinuations due to any drug-related adverse events to date. Grade 3 drug related events occurred in three patients (16.7%); and an overall five (27.8%) remained on study for at least four cycles of treatment with CB-839. We remain encouraged by the preliminary results and look forward to reviewing the data at EHA.

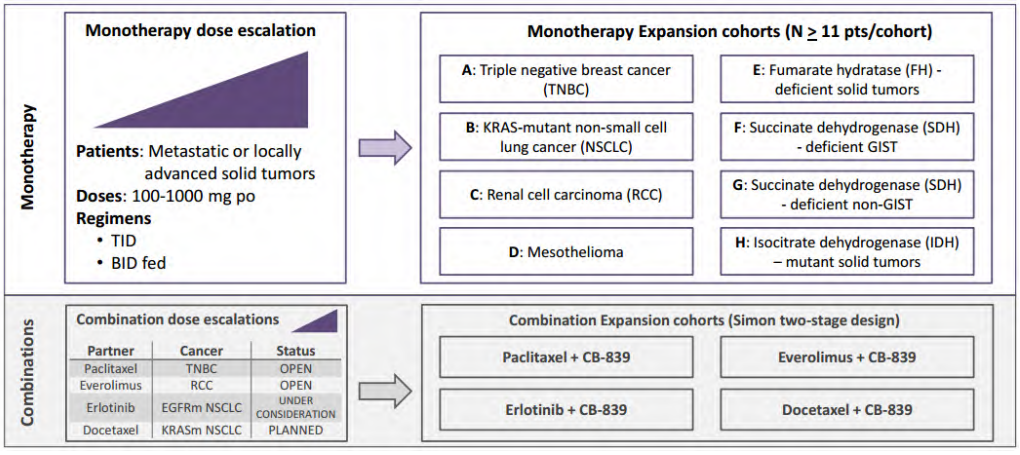
We remain bullish on CALA. Calithera is an early-stage, oncology-focused, drug discovery and development company attempting to exploit the increasing knowledge of the cancer cell's ability to hijack the energy production mechanisms required for the utilization of energy from a variety of sources. The company's first product candidate, CB-839, is a first-in-class and 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. We are also excited about the company's program in arginase inhibition, which could potentially have a role in the immuno-oncology space in much the same way as IDO inhibitors have had in the inhibition of tryptophan and its attendant effect on T-regulatory (Treg) cells. 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, sold to Amgen (AMGN, NC) in 2013 for $10 billion.

FIGURE 1. Upcoming Milestones

Timing	Drug	Catalyst
1H15	CB-839	Anticipated presentation of CB-839 (single agent) Phase I safety and efficacy in heme tumors
1H15	CB-839	Initiation of Phase Ib combo expansion trials (TNBC + paclitaxel)
mid-2015	CB-839	Initiation of Phase Ib combo expansion trials (R/R MM + pomalidomide)
2H15	Arginase Inhibitor	IND filing for arginase inhibitor
2H15	CB-839	Additional data from Phase I single agent trials in solid and heme tumors
2H15	CB-839	Initial data from Phase I combination trials
mid-2016	CB-839	Complete data from combination Phase I trials

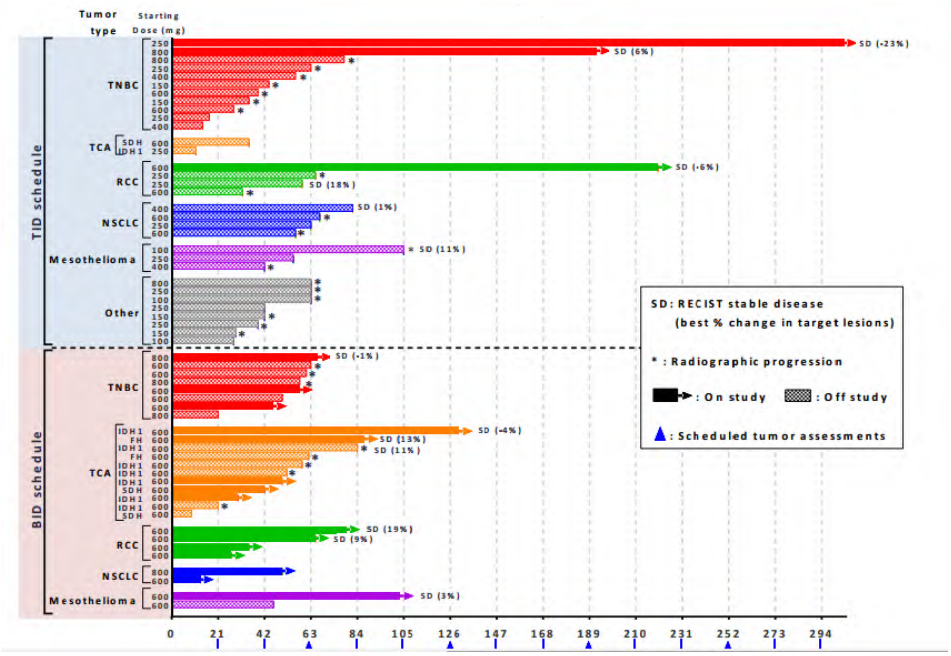
Source: Company presentations

FIGURE 2. CB-839 Study Design



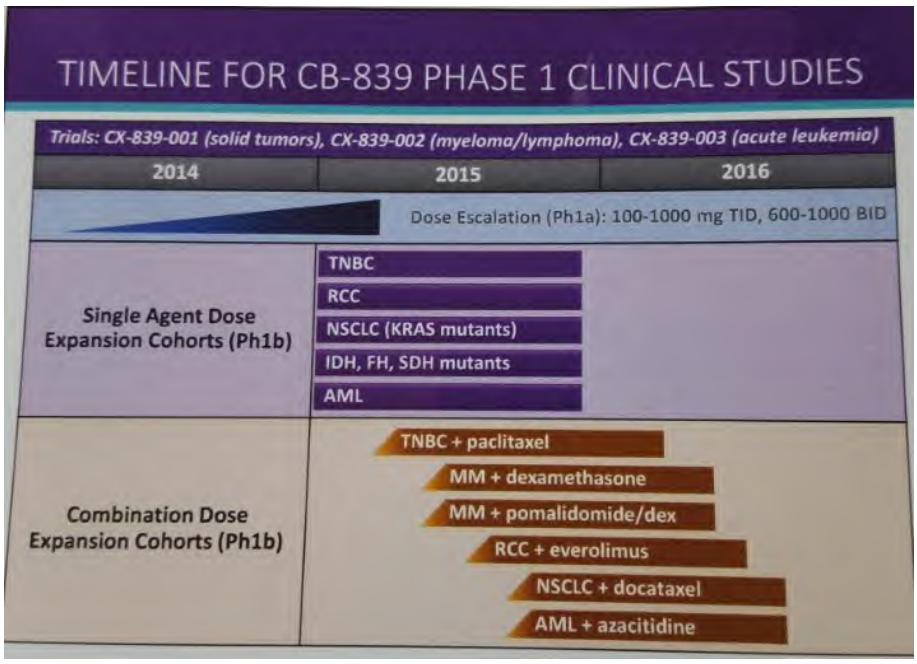
Source: ASCO 2015

FIGURE 3. Treatment Duration



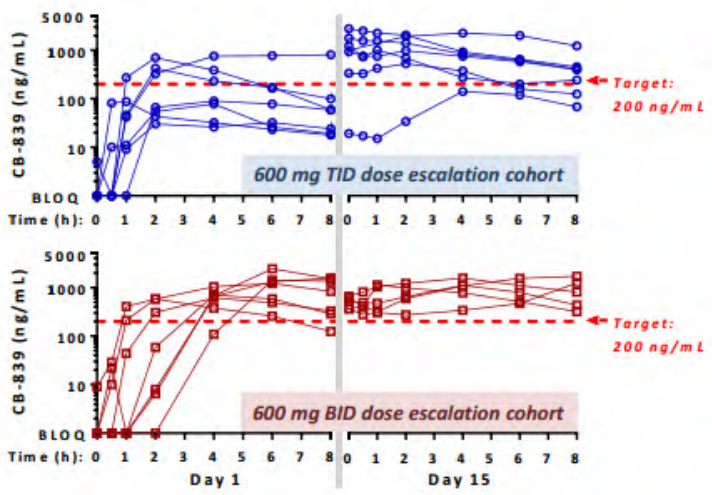
Source: ASCO 2015

FIGURE 4. Timeline for CB-839 Clinical Trials



Source: Company Reports

FIGURE 5. PK Variability is Reduced with BID Fed Dosing Regimen



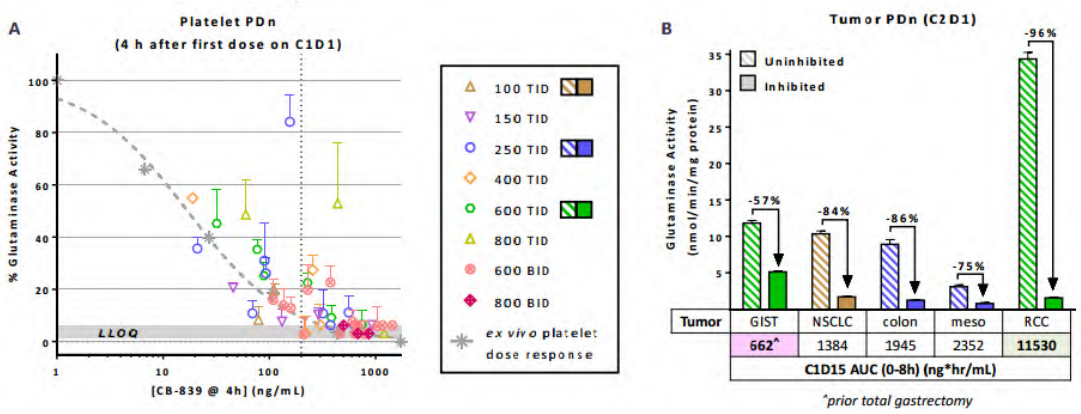
Source: ASC O2015

FIGURE 6. More Consistent Exposure with BID Fed Dosing Regimen

	Dose (mg)	100	150	250	400	600	800	600
	Schedule	TID	TID	TID	TID	TID	TID	BID
	N	3	4	10	3	7	3	8
AUC (0-8h) (ng*hr/mL)	Average	1980	7167	3852	3959	6125	5575	6201
	Variation (%CV)	33%	98%	101%	46%	70%	72%	34%
C_{max} (ng/mL)	Average	432	1467	778	846	1366	1019	1291
	Variation (%CV)	46%	87%	89%	38%	68%	35%	23%
C_{min} (ng/mL)	Average	134	585	241	306	400	457	366
	Variation (%CV)	32%	108%	105%	80%	98%	92%	35%

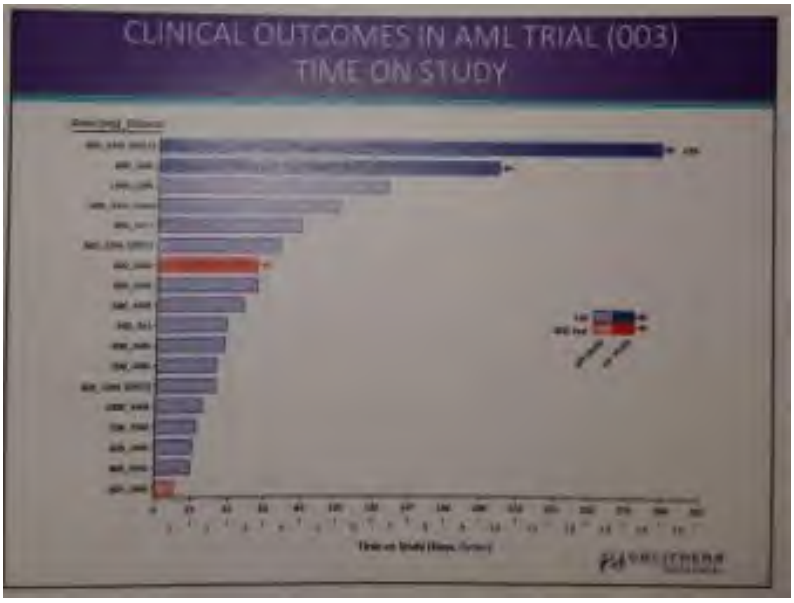
Source: ASCO 2015

FIGURE 7. Platelet and Tumor Pharmacodynamics



Source: ASCO 2015

FIGURE 8. Clinical Outcomes in AML Trial



Source: Company Reports

FIGURE 9. CALA Income Statement

Income Statement ($MM)	1Q15A	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	5.6	6.5	7.3	8.0	27.4	54.9	109.7	170.1	221.1	265.3	291.8	321.0	353.1	388.4	427.3
% Growth					*66.5%*	*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%*	*42%*	*30%*	*25%*	*24%*	*25%*	*26%*
General and administrative	2.2	2.2	2.3	2.4	9.1	20.1	60.3	108.5	157.4	196.7	216.4	235.9	254.8	267.5	280.9
Total operating expenses	7.9	8.7	9.6	10.4	36.6	75.0	170.0	278.6	378.5	462.0	508.2	556.9	607.9	655.9	708.2
Operating income (loss)	(7.9)	(8.7)	(9.6)	(10.4)	(36.6)	(75.0)	(170.0)	(230.6)	(98.9)	129.1	427.6	692.3	859.4	920.8	941.0
Operating margin (%)								*-422.5%*	*-31.2%*	*19.4%*	*40.7%*	*49.4%*	*52.3%*	*52.2%*	*51.1%*
Interest income															
Interest expense															
Total other income, net	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pretax income (loss)	(7.9)	(8.7)	(9.6)	(10.4)	(36.6)	(75.0)	(170.0)	(230.6)	(98.9)	129.1	427.6	692.3	859.4	920.8	941.0
Income tax benefit (provision)					0.0	0.0	0.0	0.0	4.9	(12.9)	(85.5)	(207.7)	(300.8)	(322.3)	(329.3)
Tax Rate									*5%*	*10%*	*20%*	*30%*	*35%*	*35%*	*35%*
Comprehensive income (loss)	(7.9)	(8.7)	(9.6)	(10.4)	(36.6)	(75.0)	(170.0)	(230.6)	(94.0)	116.2	342.1	484.6	558.6	598.5	611.6
Basic EPS to common shareholders	$ (0.40)	$ (0.42)	$ (0.43)	$ (0.44)	$ (1.69)	$ (3.31)	$ (6.12)	$ (6.95)	$ (2.70)	$ 3.17	$ 8.90	$ 12.01	$ 13.19	$ 13.46	$ 13.10
Diluted EPS to common shareholders	$ (0.40)	$ (0.42)	$ (0.43)	$ (0.44)	$ (1.69)	$ (3.31)	$ (6.12)	$ (6.95)	$ (2.70)	$ 3.17	$ 8.90	$ 12.01	$ 13.19	$ 13.46	$ 13.10
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: Company Reports & JMP Securities LLC

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-839 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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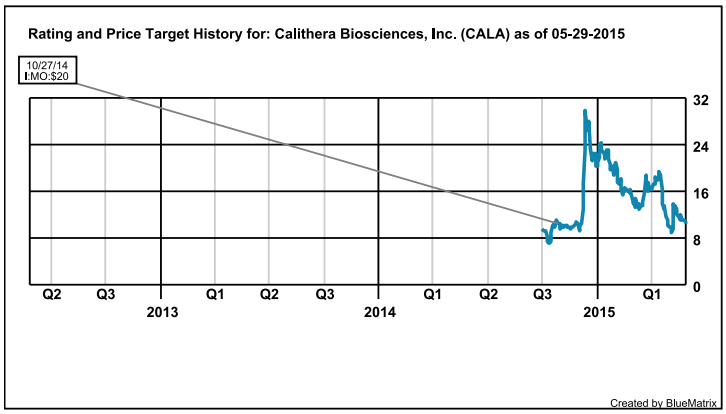
JMP Rating	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	# Co's Receiving IB Services in Past 12 Months	*% of Co's With This Rating*
MARKET OUTPERFORM	Buy	281	*62.31%*	Buy	281	*62.31%*	90	*32.03%*
MARKET PERFORM	Hold	140	*31.04%*	Hold	140	*31.04%*	17	*12.14%*
MARKET UNDERPERFORM	Sell	9	*2.00%*	Sell	9	*2.00%*	0	*0%*
COVERAGE IN TRANSITION		21	*4.66%*		21	*4.66%*	4	*19.05%*
TOTAL:		451	*100%*		451	*100%*	111	*24.61%*

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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Jeffrey H. Spurr
Director of Research
(415) 835-3903

RESEARCH PROFESSIONALS

FINANCIAL SERVICES

Alternative Asset Managers
Devin Ryan (212) 906-3578
Brian McKenna (212) 906-3545

Commercial & Specialty Finance
Christopher York (415) 835-8965
Andrius Ellner (415) 835-8962

Consumer Finance
David M. Scharf (415) 835-8942
Douglas Greiner (212) 906-3525

Financial Processing & Outsourcing
David M. Scharf (415) 835-8942
Douglas Greiner (212) 906-3525

Insurance
Matthew J. Carletti (312) 768-1784
Christine Worley (312) 768-1786
Solomon Mindlin (212) 768-1788

Investment Banks & Brokers
Devin Ryan (212) 906-3578
Brian McKenna (212) 906-3545

Mortgage Operating Companies
REITs: Agency, Hybrid, & Commercial Mortgage
Steven C. DeLaney (404) 848-7773
Trevor Cranston, CFA (415) 869-4431
Charter Robinson (757) 613-8955
Benjamin Zucker (212) 906-3529

HEALTHCARE

Animal Health
J. T. Haresco, III, PhD (415) 869-4477

Biotechnology
Liisa A. Bayko (312) 768-1785
Masha Chapman (415) 835-8944
Bhumika Sharma, PhD (312) 768-1795
Jason N. Butler, PhD (212) 906-3505
Harry Jenq, PhD (212) 906-3509
Nazibur Rahman (212) 906-3519
Michael G. King, Jr. (212) 906-3520
Bryan Czyzewski, PhD (212) 906-3577
Eric Ekland (212) 906-3540
Naureen Quibria, PhD (212) 906-3514

Healthcare Services & Facilities
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Brian Riley (415) 835-8908

Life Science Tools & Diagnostics
J. T. Haresco, III, PhD (415) 869-4477

Medical Devices & Supplies
David Turkaly (212) 906-3563
John Gillings (212) 906-3564

Specialty Pharmaceuticals

REAL ESTATE

Housing & Land Development
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Bharathwajan Iyengar (415) 835-3902

Lodging & Leisure
Robert A. LaFleur (212) 906-3510
Whitney Stevenson (212) 906-3538

Property Services
Mitch Germain (212) 906-3546
Peter Lunenburg (212) 906-3537

REITs: Healthcare, Residential, & Specialty
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Brian Riley (415) 835-8908

REITs: Office, Industrial, & Diversified
Mitch Germain (212) 906-3546
Peter Lunenburg (212) 906-3537

Residential Services
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Bharathwajan Iyengar (415) 835-3902

TECHNOLOGY

Internet Security & Communications Infrastructure
Erik Suppiger (415) 835-3918
John Lucia (415) 835-3920

Internet & Digital Media
Ronald V. Josey III (212) 906-3528
Ignatius Njoku (415) 835-8960
Andrew Boone, CFA (415) 835-3957
Shweta Khajuria (415) 835-8916

Software
Patrick Walravens (415) 835-8943
Peter Lowry (415) 869-4418
Mathew Spencer (415) 835-8930
Greg McDowell (415) 835-3934
Rishi Jaluria (415) 835-3961

Wireless & Cloud Computing Technologies
Alex Gauna (415) 835-8998

ADDITIONAL CONTACTS

Thomas R. Wright
Director of Equities
(212) 906-3599

Thomas Healy
Head of Institutional Sales
(212) 906-3533

600 Montgomery Street, Suite 1100
San Francisco, CA 94111
www.jmpsecurities.com