December 15, 2014

WELLS FARGO SECURITIES

Equity Research

Calithera Biosciences, Inc.

CALA: Stage Set For Important 2015 With Multiple CB-839 Readouts

Outperform / V

Sector: Biotechnology
Market Weight

- **Summary:** Over the last week, Calithera's shares have appreciated about 182% (vs. -2.9% for the Amex BTK and -2.8% for the S&P 500), driven in part, in our view, by preclinical data presented at the American Society of Hematology (ASH) Meeting and San Antonio Breast Cancer Symposium (SABCS), a well-attended investor event at the ASH Meeting, and growing appreciation for Calithera's lead compound CB-839 in solid tumors and blood cancers. On the heels of this strong recent share price appreciation, Calithera's share price exceeding the top end of our valuation range by about 50%, and with initial Phase I data in solid tumors to be presented at the ASCO Meeting in June and Ph. I(b) combination data in triple-negative breast cancer (TNBC) and end-stage multiple myeloma (MM) later next year, 2015 appears set up for multiple potential catalysts for CALA shares and further potential validation of CB-839's promising but early Ph. I profile. As a result, we are taking this opportunity to update our model and valuation for Calithera. We believe Calithera remains under-valued based on the long-term potential/promise of CB-839 in TNBC and MM, rare Kreb's cycle enzyme driver mutations (e.g., IDH 1 and 2), and in combination with validated cancer signaling pathway agents (e.g., EGFR/PI3K/mTOR). Based on adjustments to our model, our range increases to $50-55 from $19-20. This new 12-month valuation range implies a $1B market cap following data at the 2015 ASH Meeting and SABCS.
- **Top-level recap of our investment thesis and initiation highlights.** We initiated coverage on CALA on October 27, 2014, (initiation report available upon request) based on the promising, albeit early Ph. I profile of Calithera's glutaminase inhibitor, CB-839, in blood cancers and solid tumors. Key aspects of our investment thesis include: (1) CB-839 appears to be the 1st glutaminase inhibitor with an acceptable CNS safety profile as no cases of CNS toxicity--the Achilles' heel of prior inhibitors--have been observed to date. This side effect historically developed rapidly (usually during the 1st cycle of dosing) and was extremely debilitating (generally needed dose reduction and led to discontinuations). No CNS toxicity with CB-839 to date is an encouraging sign, in our view. (2) 2015 to be a key year for defining CB-839's profile as Ph. I monotherapy data will be presented at the ASCO Meeting and Ph. I(b) combination data in MM (CB-839+pomalidomide+dex) and TNBC (CB-839+paclitaxel) will be presented at the 2015 ASH Meeting and SABCS in December. (3) Experienced management team from Proteolix leveraging its prior experience developing Kyprolis. This experience has been evident, in our view, in CB-839's broad preclinical development program, identification and development of a novel PD assay, and CB-839's clinical development strategy, which could position the drug to enter Ph. II (potentially pivotal studies) by mid-2016). (4) Pipeline highlighted by immuno-oncology asset, an arginase inhibitor, expected to enter the clinic in 2016. *(Continued on following page.)*

Valuation Range: $50.00 to $55.00 from $19.00 to $20.00
We blend a sum-of-parts valuation using P/S multiples of 4.5-6.5x and P/E multiples of 32-37x applied to 2025E revenue of ~$500MM and EPS of $6.18, discounted at 15-18%. Key risks include clinical trial failure, a safety signal for CB-839, and financing risk.

Investment Thesis:
We believe CALA is under-valued based on CB-839's long-term potential in end-stage myeloma and triple-negative breast cancer.

Valuation Range Change

EPS	2013A	2014E Curr.	2014E Prior	2015E Curr.	2015E Prior
Q1 (Mar.)	NE	NE A		($0.34)	NC
Q2 (June)	NE	(1.22) A	NC	(0.37)	NC
Q3 (Sep.)	(34.21)	(16.85) A	NC	(0.40)	NC
Q4 (Dec.)	NE	(0.33)	NC	(0.44)	NC
FY	($3.03)	($2.40)	NC	($1.56)	NC
CY	($3.03)	($2.40)		($1.56)	
FY P/EPS	NM	NM		NM	
Rev.(MM)	$0	$0		$0	

Source: Company Data, Wells Fargo Securities, LLC estimates, and Reuters
NA = Not Available, NC = No Change, NE = No Estimate, NM = Not Meaningful
V = Volatile, = Company is on the Priority Stock List

CALA has only provided Q3 and FY 2013 EPS.
2014 quarters may not sum to our annual EPS estimate due to differences in shares outstanding and rounding.

Ticker	CALA
Price (12/12/2014)	$29.85
52-Week Range:	$6-26
Shares Outstanding: (MM)	17.9
Market Cap.: (MM)	$534.3
S&P 500:	2,002.33
Avg. Daily Vol.:	145,095
Dividend/Yield:	$0.00/0.0%
LT Debt: (MM)	$0.0
LT Debt/Total Cap.:	0.0%
ROE:	NM
3-5 Yr. Est. Growth Rate:	75.0%
CY 2014 Est. P/EPS-to-Growth:	NM
Last Reporting Date:	11/14/2014 Before Open

Source: Company Data, Wells Fargo Securities, LLC estimates, and Reuters

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All estimates/forecasts are as of 12/15/14 unless otherwise stated.

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- **Abstract at the San Antonio Breast Cancer Symposium highlights Calithera's novel pharmacodynamics (PD) assay, and confirmation of glutaminase inhibition by CB-839 in human tumor biopsy samples**. Late last week, Calithera presented a preclinical abstract describing its PD assay currently in use in its ongoing Ph. I studies. While the abstract primarily focused on CB-839's effects on glutaminase inhibition in TNBC tumor lysates and xenograft tumors, Calithera also included data from tumor biopsy samples provided by patients in the Ph. I solid tumor study. The three voluntary biopsy samples were provided by mesothelioma, colorectal, and non-small cell lung cancer patients and demonstrated reduction of glutaminase levels of 76-84% on day 1 of cycle 2 (day 22 of dosing; each cycle is 21 days). We note the mesothelioma patient described in this abstract is not the same mesothelioma patient described in the S-1, who had achieved disease stabilization for five cycles. These biopsy data are important as they represent the initial proof-of-concept in humans that CB-839 is significantly reducing glutaminase levels *in vivo*, consistent with the litany of preclinical data Calithera has published to date. As part of the Ph. I expansion cohort expected to start by year-end/early 2015 in TNBC patients, tumor biopsies will be prospectively collected from all enrolled patients to assess CB-839's impact on glutaminase levels in these patients.

Note: The following bullets were included in our "ASH 2014 Weekend Highlights" note, dated 12/8/2014.

- **The enzyme, pyruvate carboxylase may serve as a potential biomarker for identifying multiple myeloma patients more likely to respond to treatment with CB-839.** During Sunday (12/7) and Monday (12/8) Calithera presented four preclinical abstracts describing CB-839 in AML and MM. #3439 described CB-839's monotherapy profile in MM cell lines, #4720 described synergies for CB-839 with pomalidomide, and #3763 outlined CB-839's effects in AML. Abstract #3429 noted that MM cell lines that are resistant to CB-839 have elevated levels of pyruvate carboxylase (PC) whereas CB-839 sensitive cell lines have low levels of PC. Based on immunoblot analysis of 24 MM cell lines, PC protein levels were inversely correlated with response to CB-839. This is an important finding as PC converts pyruvate to oxaloacetate, an important Kreb's cycle intermediate needed for creation of energy and biomass macromolecules, both important for cancer cell growth and survival. Longer-term Calithera may explore use of PC as a potential biomarker for selecting patients who may be more likely to respond to CB-839 (e.g., similar to ARRY using low AAG as a potential biomarker to identify MM patients more likely to respond to filanesib). Currently Calithera is enrolling R/R MM patients regardless of high or low PC expression so that it can determine what response rates and safety are in all MM patients treated with CB-839.

- **CB-839 Ph. I monotherapy studies progressing well, Calithera appears on track to meet its previously announced timelines, and next major update on Ph. I data should occur at ASCO.** We attended the Calithera investor event on Saturday evening (12/6) where we had a chance to speak to management about its lead program, CB-839. The three Ph. I monotherapy studies have been recruiting well and Calithera is on track by year-end to complete study recruitment (CX-839-001 in solid tumors, -002 in MM and NHL, and -003 in ALL and AML) and to select the go-forward b.i.d. dose (CB-839 is currently dosed as t.i.d.) as part of cohort expansion for the three studies. The go-forward dose will also be used in the two Ph. I(b) combination studies for CB-839+paclitaxel in TNBC and CB-839+pomalidomide+dexamethasone in MM, both of which remain on track to start in early 2015. Similar to 2014, preclinical abstracts for CB-839 have been submitted to the Keystone Symposium in January and the AACR Meeting in April. The next major data update for the ongoing Ph. I monotherapy studies will likely be at the ASCO Meeting.

- **Agios' AG-221 in IDH2 blood cancers (AML/MDS) provides a potential read-through to CB-839 in AML?** While we don't cover Agios, Ph. I/II data presented on 12/7/12 in 45 evaluable patients with the IDH2 (isocitrate dehydrogenase) mutation appear extremely compelling with a 56% ORR including 15 patients with CR/CRi, 10 PR, 17 SD, and only two cases of progressive disease; 90% of patients had durations of response beyond three months. Based on CB-839's mechanism of inhibiting glutaminase, which is up-stream of alpha-ketoglutarate (and IDH) in the TCA (Kreb's) cycle, theoretically the glutaminase inhibitor could also elicit responses in IDH1 and IDH2 mutated cancers. As part of its ongoing Ph. I solid tumor study Calithera is studying CB-839's impact on tumors which harbor rare TCA cycle enzyme driver mutations (such as IDH, succinate dehydrogenase, and fumarate hydratase). These data along with the Ph. I data in AML (study CX-839-003) should help determine Calithera's development path in these TCA cycle enzyme driver mutations, including IDH1 and IDH2.

Exhibit 1. Calithera's Upcoming Milestones Chart

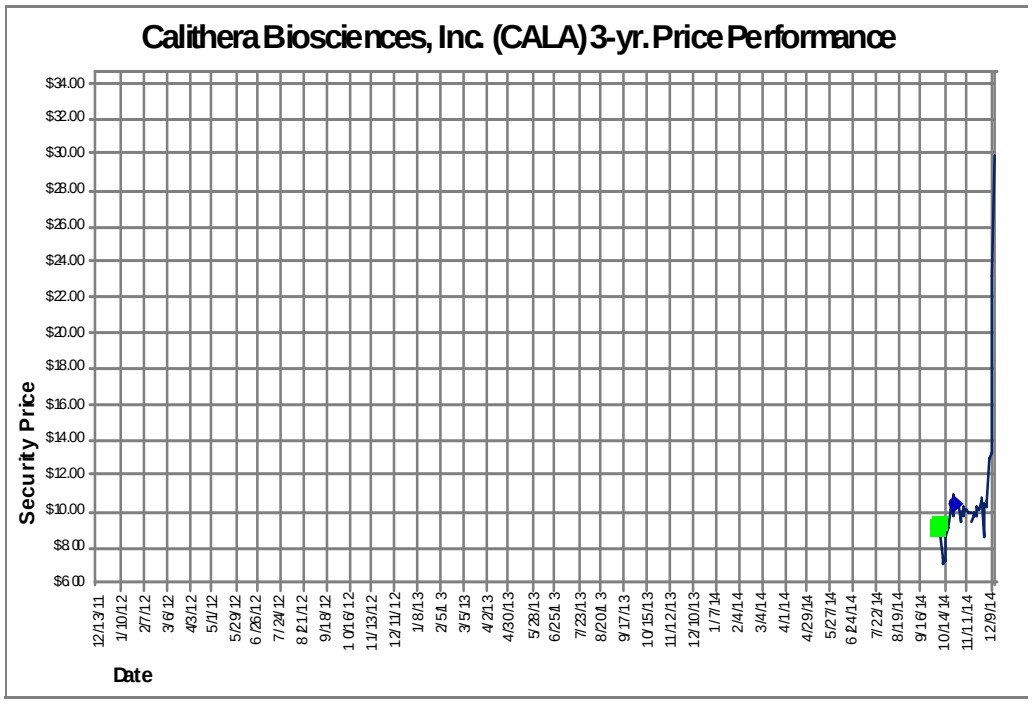
Agent	Timing	Event
CB-839	Q4 2014	Elect dose for Phase I(b) combination studies.
	End 2014	Complete enrollment for the three Ph. I monotherapy studies and initiate the Ph. I(b) combination studies for Triple Negative Breast Cancer (with paclitaxel) and multiple myeloma (with Pomalyst/dexamethasone).
	January 13-18, 2015	Present additional pre-clinical data at the Keystone Symposium (Vancouver, Canada). Dr. Bernardinis to present abstract/analysis on CB-839 and cancer cell metabolism.
	Late March/early April 2015	Report Q4 2014 earnings and provide a corporate update on pipeline.
	April 18-22, 2015	Present additional pre-clinical data at the AACR Meeting (Philadelphia, PA).
	May 29 - June 2, 2015	Present the initial Ph. I monotherapy efficacy/safety data at the ASCO Meeting (Chicago, Illinois).
	September 23-26, 2015	Present Ph. I monotherapy data in MM at the IMW Meeting (Rome, Italy)?
	December 5-9, 2015	Present the Ph. I monotherapy and combination data for the MM/NHL and ALL/AML studies at the ASH Meeting.
	December 8-12, 2015	Present the Ph. I combination data for the TNBC study at the SABCS.
	End 2015	Report the Ph. I monotherapy and combination data for the solid tumor studies.
	End 2015/Q1 2016	Complete the Ph. I monotherapy and Ph. I(b) combination studies.
	End 2015/Q1 2016	Meet with FDA (and CHMP/EMA) to discuss Ph. I(a)/(b) data and Ph. II protocols.
	Q2 2016	Initiate the Ph. II randomized studies in TNBC and MM (and possibly other solid tumors including those with rare driver mutations). Both studies to potentially include 100's of patients.
	End 2017/H1 2018	Complete the Ph. II randomized studies in TNBC and MM.
	2018	Initiate Ph. III studies in TNBC and MM.
Arginase Inhibitor	2014/2015	Complete various preclinical toxicology and other studies.
	End 2015/early 2016	Submit the INDA to regulatory agencies.
	H1 2016	Initiate a Ph. I clinical program.

Source: Company reports and Wells Fargo Securities, LLC estimates

Company Description:

Calithera Biosciences, Inc. (South San Francisco, California) is engaged in the research, development, and commercialization of small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancers. Calithera's lead program is CB-839, an oral inhibitor of the glutaminase enzyme, and is currently in three Phase I studies and plans to initiate a Ph. II program in triple-negative breast cancer and multiple myeloma in early 2016. Behind CB-839 Calithera has a pre-clinical arginase inhibitor compound which is expected to enter human studies in early 2016.

Required Disclosures



	Date	Publication Price ($)	Rating Code	Val. Rng. Low	Val. Rng. High	Close Price ($)
❐	10/3/2014		IPO at $10.00			
	10/27/2014		Andrews			
◆	10/27/2014	11.04	1	19.00	20.00	10.40

Source: Wells Fargo Securities, LLC estimates and Reuters data

Symbol Key

▼	Rating Downgrade	◆	Initiation, Resumption, Drop or Suspend
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●	Valuation Range Change	❐	Split Adjustment

Rating Code Key

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CALA: Key risks include clinical trial failure, a safety signal for CB-839, and financing risk.

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