October 27, 2014

WELLS FARGO SECURITIES

Equity Research

Calithera Biosciences, Inc.

CALA: We Have Initiated Coverage With an Outperform Rating
CB-839: Novel Cancer Therapy Targeting Cancer Cell Metabolism

Outperform / V

Sector: Biotechnology
Market Weight

Initiation of Coverage

- **Summary:** We have initiated coverage of Calithera with an Outperform rating and a $19-20 valuation range. We see CALA as an attractive, early-stage hematology/oncology company that is positioned to become a leading player in cancer cell metabolism, an area of significant research interest. We are encouraged by early Phase I data for CB-839, an oral inhibitor of glutaminase, and believe 2015 updates will further define its early but promising profile, long-term potential, and paths to market in solid tumors/blood cancers. Our valuation range is based on a sum-of-parts analysis using out-year sales multiples adjusted for probabilities of success in triple-negative breast cancer and multiple myeloma.

- **CB-839: the first glutaminase inhibitor to thread the needle on efficacy and safety?** CB-839 inhibits glutaminase, the essential enzyme needed for conversion of glutamine to glutamate, which is a key nutrient for creation of energy and TCA cycle intermediates needed to support cancer cell growth and survival. Initial Ph. I dose-escalation monotherapy data suggest signals of activity, but most important, a tolerable profile with no CNS toxicity -- the Achilles' heel of prior glutaminase inhibitors. We believe the three solid tumor/blood cancer Ph. I studies are well designed and that their adaptive designs should allow for rapid movement into Ph. I(b) TNBC and MM combination studies by late 2014 and Ph. II by 2016. A novel PD biomarker assay may allow for identification of patients most likely to respond to CB-839, increasing the likelihood of Ph. II/III success.
- **The year 2015 to be key for defining CB-839's profile and providing catalysts for CALA.** The initial detailed look at monotherapy data should occur at the AACR and/or ASCO Meetings, with important Ph. I(b) TNBC and MM combination studies data expected by the end of 2015. In addition, monotherapy data should dictate if CB-839 can be used to treat rare orphan cancers that harbor TCA cycle enzyme driver mutations, which may offer faster paths to market.
- **Experienced management team leveraging Kyprolis success.** A number of CALA senior management were involved in Kyprolis' development while at Proteolix, acquired by Onyx in 2009. We believe this prior experience is highly leverageable and has been evident, in our view, for CB-839 based on a thorough and broad pre-clinical program, well-designed Ph. I/II studies and long-term strategy, identification and ongoing validation of a novel biomarker assay, and involvement of key U.S. investigators in solid tumors and blood cancers.
- **Pipeline highlighted by immuno-oncology pre-clinical asset, to enter Ph. I in 2016.** CALA's arginase inhibitor may enable re-activation of the body's cytotoxic T-cells. Theoretical proof-of-principal exists from IDO inhibitors, where antagonism allows for re-expression of tryptophan to activate T-cells.

Valuation Range: $19.00 to $20.00 from NA to NA
Our sum-of-parts valuation uses P/S multiples of 4.0-5.5x applied to 2025E revenue of $398MM discounted at 18-20%. 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.

EPS	2013A	2014E Curr.	2014E Prior	2015E Curr.	2015E Prior
Q1 (Mar.)	NE	NE A	NC	($0.34)	NE
Q2 (June)	NE	(1.22) A	NC	(0.37)	NE
Q3 (Sep.)	NE	(0.28)	NE	(0.40)	NE
Q4 (Dec.)	NE	(0.31)	NE	(0.44)	NE
FY	($3.03)	($1.39)	NE	($1.63)	NE
CY	($3.03)	($1.39)		($1.63)	
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 not provided Q1 to Q4 2013 EPS, only full-year 2013 EPS.
CALA has not provided Q1 or Q2 EPS, only H1 2014 EPS.
Loss per share in H1 2014 was -$1.22.
Due to rounding and use of diluted share count the sum of Q1 to Q4 does not equal FY 2015 EPS.

Ticker	CALA
Price (10/24/2014)	$11.04
52-Week Range:	$6-12
Shares Outstanding: (MM)	17.9
Market Cap.: (MM)	$197.6
S&P 500:	1,964.58
Avg. Daily Vol.:	0
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:	NE
CY 2014 Est. P/EPS-to-Growth:	NM
Last Reporting Date:	06/30/2014

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

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Please see page 38 for rating definitions, important disclosures and required analyst certifications

All estimates/forecasts are as of 10/27/14 unless otherwise stated.

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.

Investment Summary

We have initiated coverage of CALA with an Outperform rating and a $19-20 valuation range. We believe Calithera's approach to targeting cancer cell metabolism by blocking the effects of glutaminase, an important enzyme involved in the processes for creation of energy and Tricarboxylic Acid (TCA/Kreb's) cycle intermediates, which are needed for cancer cell survival and growth, has strong scientific rationale; and pre-clinical and early human proof-of-concept data suggest that its lead compound CB-839 has a promising, though early profile that avoids many of the key safety issues which have historically plagued prior glutaminase inhibitors. The year 2015 should be key in defining CB-839's profile and long-term potential (in multiple solid tumors and blood cancers), and in our view, offers the potential for share appreciation as more detailed Phase I monotherapy and combination study data emerge by the middle and end of 2015, respectively. Behind CB-839, Calithera's pre-clinical arginase inhibitor is expected to enter Ph. I human study in 2016 and offers the potential for the company to become involved in the exciting area of immuno-oncology. We see Calithera as an attractive investment idea in the cancer metabolism/immuno-oncology fields.

Inhibition of glutaminase offers an attractive target for the treatment of cancer. Over the past few decades, interest in cancer cell/tumor metabolism has enjoyed revitalized interest as an area of key scientific research as it has become clear that cancer cells' metabolic phenotype is linked to mutations in oncogenes and tumor suppressor genes. As a result of the genetic "re-wiring" of cancer cells' machinery, their reliance on glucose as a key source for generation of energy and the TCA cycle intermediates needed for creation of biomass macromolecules (e.g., amino acids, nucleotides, and proteins) decreases while their reliance on glutamine as the key source for bioenergetic and biosynthetic needs increases. CB-839 selectively blocks the effects of glutaminase, a mitochondrial enzyme that converts glutamine to glutamate and, as a result, the cancer cell has less glutamate (e.g., the fuel) to meets its bioenergetic and biosynthetic needs. In addition to depriving the cancer cells of a key fuel source, lower levels of antioxidant glutathione are produced by glutamate, which results in the cancer cell's diminished ability to combat reactive oxygenated species (ROS). As a result, CB-839 may induce cancer cell death in two complementary ways.

While early in development, initial CB-839 data suggest signals of activity, but more important, no neurological toxicity has been observed. CB-839 is progressing in the dose-escalation phase of three Ph. I monotherapy studies in the following: (1) advanced solid tumors, (2) multiple myeloma/non-Hodgkin's lymphoma (MM/NHL), and (3) acute lymphoblastic leukemia/acute myeloid leukemia (ALL/AML). To date, four cases of disease stabilization have been observed in MM (two cases), mesothelioma (one case), and triple-negative breast (TNBC; one case), including the TNBC patient whose tumor shrank 13%. While we expect response rates should improve through monotherapy dose-escalation and during 2015, when the Ph. I(b) combination studies are under way with the go-forward Ph. II/III dose, most important, in our view, is that CB-839's adverse event (AE) profile to date appears very manageable, with only two Grade 3 events and no cases of central nervous system (CNS) toxicity. Unlike prior glutaminase inhibitors, CB-839 does not efficiently cross the blood-brain-barrier (BBB) and binds non-covalently at an allosteric site and, as a result, has avoided key neurotoxic side effects that halted the development of prior compounds azaserine, acivicin, and DON (6-Diazo-5-oxo-L-norleucine). CNS toxicity has historically been the AE that has halted development of previous glutaminase inhibitors. This toxicity was observed early, generally in cycle 1, and was extremely debilitating, usually Grade 3 or 4. While we await more complete Ph. I data in 2015, the lack of any CNS toxicity to date and CB-839 being dosed at 600mg in one of the studies, which is approaching the high end of the expected dosing range (about 800 mg), suggest to us that CB-839 may on the right path of successfully threading the needle for an efficacious compound without any CNS toxicity.

We believe the clinical program is well designed, allows for rapid advancement into Ph. II by 2016, and that it potentially will identify patients more likely to respond to CB-839. Upon defining the go-forward dose later in 2014 (expected by Calithera to be the same for both solid tumors and blood cancers), Calithera plans to initiate two Ph. I(b) combination studies in TNBC (in combination with paclitaxel) and R/R MM (in combination with Pomalyst/dexamethasone) (see Exhibit 12). The studies are designed to allow for an increase or decrease in the sample size based on early signals of activity and safety. Randomized and confirmatory Ph. IIs in TNBC and MM are expected to commence in 2016. Calithera's strategy for pursuing both cancers is driven, in part, by (1) CB-839's pre-clinical synergies with paclitaxel and Pomalyst, (2) *in vitro/in vivo* data suggesting both cancers are highly reliant on glutamate and sensitive to glutaminase inhibition, and (3) builds upon paclitaxel and Pomalyst's usage/profile in both cancers. We believe the combination strategy in R/R MM with Pomalyst (which is quickly becoming the gold standard in patients who are refractory to both Velcade and Revlimid) is a solid one as the third Line+ market is likely to continue to grow, no therapy is curative, and we believe patients will cycle from one therapy to another. In second Line+ TNBC, the current standard of care is a clinical trial and patients' progression-free survival (PFS) is short (e.g., $\leq$ four months). Similarly, patients will likely cycle through available therapies in an attempt to slow/halt disease progression. As part of the ongoing Ph. I program, Calithera is incorporating a novel pharmacodynamics assay to assess glutaminase levels in platelets in all patients, as well as collect biopsy samples from TNBC patients. The assay should help them confirm their thesis that expression of glutaminase in serum is the appropriate biomarker to assess patients. In addition, due to the varying degrees of cancers' sensitivity to glutaminase inhibition, the assay and other gene signature analyses may allow for identification of patients more likely to respond positively to CB-839, potentially increasing the likelihood of success in Ph. II/III.

The year 2015 to be important for defining CB-839's overall product profile; and AACR, ASCO, ASH, and SABCS could offer catalysts for Calithera's shares. As of July 25, 2014, 24 patients had been recruited for the three Ph. I monotherapy studies, and the monotherapy and combination studies could recruit between 130 and potentially 200+ patients, driven by safety and efficacy results observed through the course of the studies. Due to the early nature of the monotherapy studies, limited number of patients, limited follow-up period, and the studies still being in dose-escalation (thus, some patients may have been under-dosed initially from an efficacy perspective), investors are not expected to see safety and efficacy data at the 2014 American Society of Hematology Meeting or San Antonio Breast Cancer Symposium in December. If the abstract is accepted for the ASH Meeting, Calithera plans to present MM biomarker data, suggesting pyruvate carboxylase may allow for patient selection. Beyond Calithera's S-1 document, and whether management shares limited details in upcoming earnings releases, investors should get their next detailed look at more mature monotherapy data at the AACR and/or ASCO Meeting(s) in 2015. While the Ph. I dose-escalation and maximum-tolerated dose (MTD) monotherapy data should be important to allow for potential comparison to other MM and TNBC therapies, we believe the more important data will be the Ph. I(b) combination results, which should emerge later in 2015. Since Calithera's development strategy is to combine CB-839 with approved standards of care, these combination data should help guide Calithera's Ph. II plans in terms of study size, expected treatment effect on response rates, etc.

Beyond TNBC and MM, Calithera is exploring the potential for CB-839 in cancers that have TCA cycle enzyme driver mutations. In addition to the larger solid tumor, MM/NHL, AML/ALL studies, the Ph. I protocols allow for study sites to recruit patients (about 10-15% of the solid tumor study patients) that have rare, orphan cancers that are driven by TCA cycle enzymes mutations (see Exhibit 25). In select cancers, the enzymes succinate dehydrogenase and fumarate hydratase are inactivated due to loss of function mutations resulting in accumulation of succinate and fumarate (two TCA cycle intermediates), while a gain of function mutation in isocitrate dehydrogenase (IDH) leads to increase in an oncometabolite, 2-HG. As a result, these TCA enzyme driver mutations can contribute to development of cancers, such as paraganglioma, pheochromocytoma, and AML. By blocking production of glutamate and production of these TCA cycle intermediates and oncometabolite, CB-839 may contribute to cancer cell death. While the prevalence of these cancers is low and can range from a few hundred to a few 1,000 (e.g., 3,000), a promising signal of activity and safety in the Ph. I program could offer a potentially accelerated path to market, with a single-arm, Ph. II study utilizing objective response rate (ORR) as the primary endpoint. In addition, this would accelerate CB-839's time to be market, ahead of our estimated approvals in R/R MM and TNBC, in 2021, and 2022, respectively.

Strong management team and prior success with Kyprolis provides a good financial, scientific, clinical, and regulatory foundation. Calithera's management team successfully developed and advanced Kyprolis for R/R MM into human study(ies) while at Proteolix, Inc. In 2009, Onyx acquired Proteolix for a deal valued at up to $841 million in cash, driven by the clinical promise of Kyprolis. While there is no guarantee that Calithera's management can replicate its success with Kyprolis with the development of CB-839, we believe that its basic science, clinical, and regulatory experience(s) provides the company with important credibility with investors, regulators, clinicians, and potential pharmaceutical partners, considering the complexities of drug development. We believe the prior experience with Kyprolis is highly leverageable (beyond just R/R MM) and is currently reflected in a thorough pre-clinical program and well-designed Ph. I/II studies and life-cycle management plans for CB-839.

Arginase inhibitor program could give Calithera an additional shot on goal in the promising immuno-oncology space. Complementing its Ph. I cancer metabolism program, Calithera also has a pre-clinical immuno-oncology program. Myeloid-derived suppressor cells secrete a ubiquitous enzyme, arginase, which results in the down-regulation of arginine, an amino acid important for the activation, growth, and survival of cytotoxic T-cells, which are important in the body's immune system and targeting of cancer cells. Calithera's pre-clinical compound blocks arginase, thus allowing cytotoxic T-cells to regain lost function and re-target and attack cancer cells. While little is known about the compound, clinical proof-of-principle could come from early stage inhibitors of indoleamine 2,3-doxygenase (IDO). IDO is one of several immune checkpoints that may be involved in tumor immune escape. Increased IDO expression by antigen presenting cells leads to tryptophan depletion, resulting in antigen-specific T-cell anergy and regulatory T-cell recruitment. Initial Ph. I/II data for Incyte's INCB24360 in combination with ipilimumab in metastatic melanoma and New Link Genetics' indoximod and NLG 9191 were presented at ASCO 2014. Calithera expects to file an IND in 2015 and initiate human studies by 2016.

Valuation

We have established a $19-20 valuation range for Calithera Biosciences, Inc.'s shares. We base our valuation analysis on our probability-adjusted revenue projections for CB-839 in R/R MM and TNBC, where we currently assume probabilities of success for both indications of 30%. We currently do not include approvals in any of the potential rare cancers with TCA cycle enzyme driver mutations in our valuation. We conservatively assume that Calithera will pursue more traditional sequential Ph. II and Ph. III studies for approval both in the United States and Europe in R/R MM and TNBC. As a result, we do not expect U.S. or EU approvals of CB-839 in R/R MM and TNBC until 2021 and 2022, respectively. Thus, our valuation is based on CB-839 U.S. sales, ex-U.S. royalties, and any associated milestone revenue occurring in 2025. Based on the approvals of Pomalyst and Kyprolis in R/R MM and the clinical development programs for companies targeting TNBC – such as Celldex – there may be expedited paths to market in the United States based on a well-designed, randomized Ph. II study, as well as on an interim analysis from a pivotal Ph. III study. As a result, earlier-than-expected approval(s) in the United States could offer potential upside to our current estimates and valuation. In addition, rare cancers with TCA cycle enzyme driver mutations could also offer quicker to market paths as these cancers are orphan diseases for which there is no established standard of care. In 2025, we assume $164 million and $116 million in U.S. sales in TNBC and R/R MM, and $24 million and $15 million in ex-U.S. royalties in TNBC and R/R MM, respectively for total revenue of $319 million. As noted in the following exhibit, we apply a 5.0-5.5x P/S multiple on U.S. sales discounted at 18% and a 4.0-4.5 P/S multiple on ex-U.S. royalties discounted at 20%; in addition, we include cash on hand ($79 million) as part of our sum-of-parts analysis. We discount the revenue back 10.2 years to the end of 2015 and, utilizing a fully diluted share count of about 19 million shares, we arrive at a valuation range of $19-20. In addition, our sum-of-parts analysis is supported by our price-to-sales analysis (utilizing a 15% discount rate and a 5.0-5.5x multiple) and a price-to-earnings analysis (utilizing an 18-20% discount rate and 30-35x multiples, which we think is appropriate for high-growth, small-cap biotechnology companies).

Exhibit 1. Calithera's Sum-of-Parts Valuation Analysis

CALA Sum-of-parts valuation analysis

	2025E Revenues	Discount Rate	Low Multiple	High Multiple	Low NPV	High NPV	Low value/share	High value/share
CB-839 TNBC (U.S. sales)	$164,110	18%	5	5.5	$151,810	$166,991	$7.98	$8.78
CB-839 TNBC (EU	$24,423	20%	4	4.5	$15,228	$17,131	$0.80	$0.90
CB-839 MM (U.S. sales)	$115,655	18%	5	5.5	$106,988	$117,686	$5.62	$6.18
CB-839 MM (EU royalty)	$14,679	20%	4	4.5	$9,152	$10,296	$0.48	$0.54
Net Cash	$79,380		-	-	$79,380	$79,380	$4.17	$4.17
Total	$398,247						**$19.05**	**$20.57**
Estimated Market Capitalization in 000's $.							$360,653	$389,428

Valuation Year	2025
Valuation Date	12/31/2025
Today's Date	10/24/2014

Source: Wells Fargo Securities, LLC estimates
Note: Share count is as of the end of FY 2015 (December 31, 2015). In 000's $ except for value per share.

Exhibit 2. Calithera's Price-to-Sales Valuation Analysis

CALA Price to Sales Valuation

Revenues		
Estimated 2025 CALA Revenues	$322,616	$322,616
Total Revenues	**$322,616**	**$322,616**
Multiple	**5.0**	**5.5**
Multiple*Revenues	**$1,613,082**	**$1,774,391**
Discount Rate	18%	15%
Periods	**10.2**	**10.2**
PV of Future Revenues	**$298,167**	**$426,512**
Estimated Shares Outstanding at end of 2015	19,028	19,028
Estimated Share Value	**$15.67**	**$22.42**

Source: Wells Fargo Securities, LLC estimates
Note: Shares and revenues in 000's $.

Exhibit 3. Calithera's Price-to-Earnings Valuation Analysis

Price to Earnings Valuation

Valuation Year	**2025**
Valuation Date	**12/31/2025**
Today's Date	10/24/2014
2025E EPS	**$3.92**
Years	**10.2**

P/E Multiple	Discount Rate 15%	18%	20%
25	$23.58	$18.14	$15.28
27	$25.47	$19.59	$16.50
30	$28.30	**$21.76**	**$18.34**
32	$30.18	**$23.21**	**$19.56**
35	$33.01	**$25.39**	**$21.39**
37	$34.90	$26.84	$22.61
40	$37.73	$29.02	$24.45

Source: Wells Fargo Securities, LLC estimates

Exhibit 4. Probability-Weighted CB-839 Revenue Summary

CB-839 Revenues to Calithera

	Probability	2021E	2022E	2023E	2024E	2025E
TNBC - U.S. Sales	*30%*		$8,906	$47,691	$102,154	$164,110
TNBC - EU (Royalty)	*30%*			$3,706	$11,972	$24,423
MM - U.S. Sales	*30%*	$5,432	$36,273	$53,741	$81,998	$115,655
MM - EU (Royalty)	*30%*		$2,636	$5,566	$9,757	$14,679
Other driver mutations - U.S. sales*	*0%*					
Other driver mutations - EU (royalty)*	*0%*					
Total		**$5,432**	**$47,814**	**$110,705**	**$205,881**	**$318,866**

Source: Wells Fargo Securities, LLC estimates

Note: *= not included in valuation. Revenues in 000's $.

Upcoming Milestones

Exhibit 5. Calithera's Upcoming Milestones

Agent	Timing	Event
CB-839	Q4 2014	Elect dose for Phase I(b) combination studies.
	December 5 - 9, 2014	Present data at the ASH Meeting on the novel biomarker (pyruvate carboxylase) for CB-839 in multiple myeloma patients.
	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).
	April 18 - 22, 2015	Present initial monotherapy efficacy data at the AACR Meeting (Philadelphia, PA).
	May 29 - June 2, 2015	If not at the AACR Meeting, present the initial Ph. I monotherapy efficacy/safety data at the ASCO Meeting (Chicago, Illinois).
	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	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 2013	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

Exhibit 6. Calithera's Pipeline Chart

Calithera Biosciences, Inc. Pipeline Summary		
Candidate	**Indication**	**Stage And Summary**
CB-839	Triple Negative Breast Cancer (TNBC)	**Phase I -** Study CX-839-001 will enroll up to 100 patients with TNBC and other solid tumors, such as Non-Small Cell Lung Cancer. The Phase I(b) portion of the study in TNBC will include the combination of CB-839 with paclitaxel based on preclinical studies which suggest synergistic activity. Preclinical data suggest TNBC is more sensitive to CB-839 as opposed to Estrogen receptor (ER) positive or HER2+ breast cancers. As part of the ongoing Ph. I study Calithera will collect tumor biopsies to assess glutaminase levels in order to confirm the pharmacodynamic results of its assay for glutaminase in platelets (a biomarker). These data may also help identify TNBC patients more likely to respond to CB-839.
	Multiple Myeloma (MM)	**Phase I -** The Ph. I study CX-839-002 will enroll up to 65 MM and NHL patients who failed at least two prior therapies. Preclinical data suggest synergistic activity for CB-839 with lenalidomide and pomalidomide. The Ph. I(b) study will assess the combination of CB-839/pomalidomide/dexamethasone. MM could offer a faster path to market if FDA agrees to a CB-839/pomalidomide/dexamethasone vs. pomalidomide/dexamethasone Ph. II study where objective response rate (ORR) is the primary endpoint. Europe is likely to require a more traditional Ph. III study with progression-free survival (PFS) or overall survival (OS) as the primary endpoint. Calithera has identified a (negative) biomarker (pyruvate carboxylase) for CB-839 in MM patients, which may predict response to therapy.
	Non-Hodgkin's Lymphoma (NHL)	**Phase I -** NHL patients with Waldenstrom's, Diffuse Large B-cell, and other NHL sub-types who are relapsed or refractory to two prior lines of therapy will be enrolled in the CX-839-002 study.
	Acute Myeloid Leukemia (AML)	**Phase I -** Study CX-839-003 will enroll up to 50 ALL and AML patients who have failed at least one prior therapy. Newly diagnosed patients 60 years or older can enroll if they are not candidates for stem-cell transplantation or are unfit for standard chemotherapy. AML patients with isocitrate dehydrogenase (IDH)1 and IDH2 driver mutations are allowed to enroll in the study. Unlike Agios' AG-221 which targets the mutant IDH2 protein (over-expressed in AML and gliomas) in order to stop cancer cell growth, CB-839 blocks creation of glutamate which is needed to generate alpha-ketoglutarate and its oncometabolite 2-HG, which is important for IDH2 cancer cell growth.
	Acute Lymphoblastic Leukemia (ALL)	
	Hereditary leiomyomatosis and renal cell cancer (HLRCC)	**Phase I -** Ten to fifteen percent of patients recruited into the CX-839-001 study will have TCA cycle enzyme driver mutations, characterized by loss of function gene mutations for fumarate hydratase (FH) and succinate dehydrogenase (SDH) or gain of function mutations for IDH. HLRCC is characterized by a loss of function in the FH enzyme which leads to accumulation of fumarate, which is downstream of glutamate within the TCA cycle. By inhibiting glutaminase, reactivation of the FH enzyme may lead to cancer cell death in patients with this rare cancer. Less than 1% of renal cell carcinoma patients have the HLRCC mutation.
	Gastrointestinal Stromal Tumors (GIST)	**Phase I -** GIST, paragangliomas, pheochromocytomas, and RCC are characterized by loss of function in the succinate dehydrogenase (SDH) enzyme, which leads to accumulation of succinate which is downstream of glutamate within the TCA cycle. Less than 15% of GIST patients have this mutation (~3,000 patients). The CX-839-001 protocol includes 10-15% of patients with these tumor types.
	Combination studies for solid tumors	**Discovery -** Preclinical studies suggest synergies may exist for CB-839 with various growth factor signaling pathway inhibitors of EGFR, Ras/Raf, and PI3K/mTOR in various solid tumors, such as RCC, NSCLC, sarcoma, and myeloma. This is based on the fact that cancer cell metabolism is driven in part by ongogenic transformation and/or loss of tumor suppressor gene function, which results in increasing reliance of cancer cells on glutamine. As a result, blockade of signaling pathways and glutaminase may lead to increased efficacy in a number of tumor types and blood cancers.
Arginase Inhibitor	Solid tumors	**Preclinical -** Potential proof-of-concept for inhibition of arginase has been demonstrated by Indoleamine 2, 3 doxygenase inhibitors, which antagonize the IDO enzyme, which depletes tryptophan, an amino acid important in T-cell activation. Myeloid-derived suppressor cells secrete arginase which down-regulates arginine, an amino acid important in activation, growth, and survival of cancer-fighting cytotoxic T cells. Arginine depletion has been observed in RCC, AML, breast, and pancreatic cancers. Inhibition of arginase may allow for up-regulation of arginine and restore activity of the body's cytotoxic T cells. Calithera expects to enter human studies for this program in 2016.

Source: Company reports and Wells Fargo Securities, LLC estimates

Key Risks

Clinical and development risks. Calithera's lead program CB-839 currently is in early Ph. I clinical studies for multiple solid tumors and blood cancers, while its arginase inhibitor program is in pre-clinical development. While there have been four cases of disease stabilization (including one that included tumor shrinkage of 13%) and no cases of neurotoxicity for CB-839, it is possible that even in Ph. I(b), combination studies efficacy (as measured by ORR) may not be sufficiently competitive with other development agents to warrant advancement into Ph. II and/or Ph. III. In addition, higher toxicities, clinically meaningful neurotoxicities, and an unexpected safety signal may emerge, which halts the development of CB-839. Historically severe neurotoxicity has been a key adverse event that has halted the development of previous glutaminase inhibitors.

Commercial risk. While current CEO Dr. Susan Molineaux, SVP, Development Dr. Chris Molineaux, and SVP, Research Dr. Mark Bennett helped to successfully advance Kyprolis into Ph. II development, prior to Onyx acquiring Proteolix (and then obtaining U.S. approval in 2012), Calithera's management team has limited experience in commercial operations. In order to market CB-839, Calithera may have to build a commercial organization in the United States and potentially, Europe, which requires significant financing and entails significant risk, due to the global macro-economy, healthcare budgets, and an increasingly complex reimbursement landscape.

Financing risk. Clinical drug development and establishment of commercial sales and marketing infrastructures is expensive and very challenging, in our view. Calithera's drug candidates may not be sufficiently efficacious, too toxic, or may become obsolete, due to competitors' programs, and, as a result, Calithera may be unable to successfully find a licensing partner to help development and/or market CB-839 and Calithera's other drug candidates. Thus, Calithera may have to issue additional common stock and/or convertible debt, which could lead to dilution of existing shareholders.

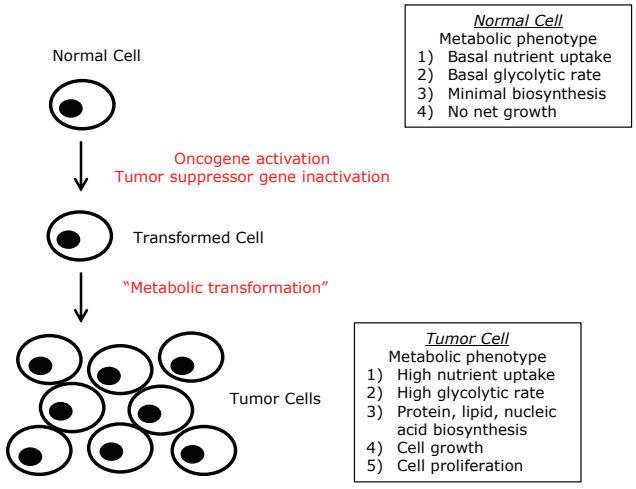
Basic Backgrounder on Cell Metabolism

Cancer cell metabolism was recognized as being different from normal cell metabolism in the early 20th Century. Nearly a century ago German physiologist Otto Heinrich Warburg observed that tumor cells consume a larger amount of glucose than normal cells and convert most of it into lactic acid. Essentially cancer cells demonstrate a high rate of glucose utilization and lactate production despite the presence of sufficient oxygen to oxidize glucose carbon in the mitochondria (aerobic glycolysis). By comparison, normal cells convert nutrients such as sugar into energy via a more efficient process in the mitochondria known as the Tricarboxylic Acid (TCA) or Kreb's cycle. Warburg's seminal work has become known as the Warburg effect and laid the foundation for one of the earliest general concepts of cancer: namely, a key disturbance of cellular metabolic activity is at the root cause of tumor formation and growth (DeBerardinis). Over the past few decades, interest in cancer cell/tumor metabolism has enjoyed revitalized interest as it has become clear that the cancer cell's metabolic phenotype is linked to genetic mutations underlying signaling pathways and tumor suppressor genes.

Metabolism, as defined by Ralph DeBerardinis and Craig B. Thompson in Mendelsohn et al.'s *The Molecular Basis of Cancer*, is the sum of the biochemical activities that allow a cell or an organism to maintain bioenergetics (processes that determine the energy state of a cell) and executive tasks. Traditionally metabolism is concerned with the handling of organic compounds -- such as sugars (carbohydrates), amino acids, nucleotides, and lipids – through a variety of enzymatic pathways (e.g., the TCA cycle). According to Vander Heiden, the study of cancer cell metabolism focuses on the enzymes and pathways used by cancer cells to transform nutrients into the chemical precursors that make up a cell, and to generate adenosine triphosphate (e.g., ATP, energy) and reducing equivalents that support cellular processes. The goal of these metabolic activities is to generate the energy and macromolecules, i.e., lipids, proteins, and nucleotides, necessary to support the cell's survival and growth needs. In addition to glycolysis and the TCA cycle, research over a series of decades has indicated that glutaminolysis (the conversion of glutamine to glutamate, and creation of substrates that replenish the TCA cycle and supply building blocks for amino acid and nucleotide synthesis) plays a critical role in cancer cell survival and growth.

Normal cells undergo metabolic transformation into cancer cells due to genetic mutations and their energy needs change accordingly. As noted in the following exhibit, normal non-proliferating cells have basal (e.g., minimal) nutrient uptake and glycolytic rates with low needs for creation of energy and macromolecules to support rapid cell growth. However, as a result of mutations in tumor suppressor genes (e.g., p53) and oncogenes (e.g., Ras, Raf, PI3K), normal cells undergo metabolic transformation and their energy demands increase into order to support growth, proliferation, and survival *(please see Exhibit 24 for more details on the various mutations in PI3K, mTOR, HIF-1α, Myc, Ras, p53, and AMPK, which highlight the important association between cancer cells' re-wired machinery of glycolysis and glutamine reliance and genetic mutations associated with the metabolic changes).* The cancer cell phenotype is characterized by (1) a high rate of glucose uptake and glycolysis; (2) a sub-optimal activity of oxidative metabolism, including the TCA cycle; (3) increased glutamine uptake and utilization; and (4) increased production of lipids and nucleic acids. Most of the increased nutrient uptake in proliferating cells is used to support biosynthetic reactions (e.g., the production of lipids, fatty acids, cholesterol, and nucleic acids).

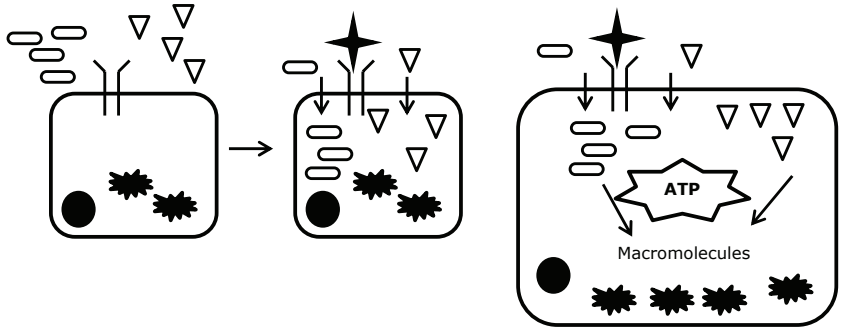
Exhibit 7. Differing Phenotypes For Normal And Tumor Cells



Source: Adapted from Mendelsohn et al. 2008 *The Molecular Basis of Cancer* and Wells Fargo Securities, LLC

As noted in Mendelsohn et al., in dormant/normal cells, uptake of nutrients like glucose and amino acids is minimal despite extracellular abundance of these substances. After a growth factor binds to its receptor on the cell surface (as depicted by the star in Exhibit 8), activation of a signal transduction pathway stimulates the cell to take up nutrients such as glucose and use them in pathways that generate energy and support the production of macromolecules needed for cell growth. In tumor cells, growth factor signal transduction pathways become constitutively active (e.g., the receptor is essentially always "on"), driving anabolic metabolism, which allows cells to produce macromolecules in the absence of cell-extrinsic stimuli. In order to double the number of macromolecules needed in a cell before mitosis, the cell needs an increased supply of basic substrates for macromolecular synthesis. A key substrate is glucose because TCA cycle intermediates in glucose metabolism contribute directly or indirectly to the synthesis of all three macromolecular classes. Due to the genetic re-wiring of cancer cells, glutamine also becomes particularly important for both biosynthesis and bioenergetics and replaces glucose as a primary substrate for these metabolic pathways.

Exhibit 8. Constitutive Activation of Growth Factor Signaling Drives Cancer Cell Growth



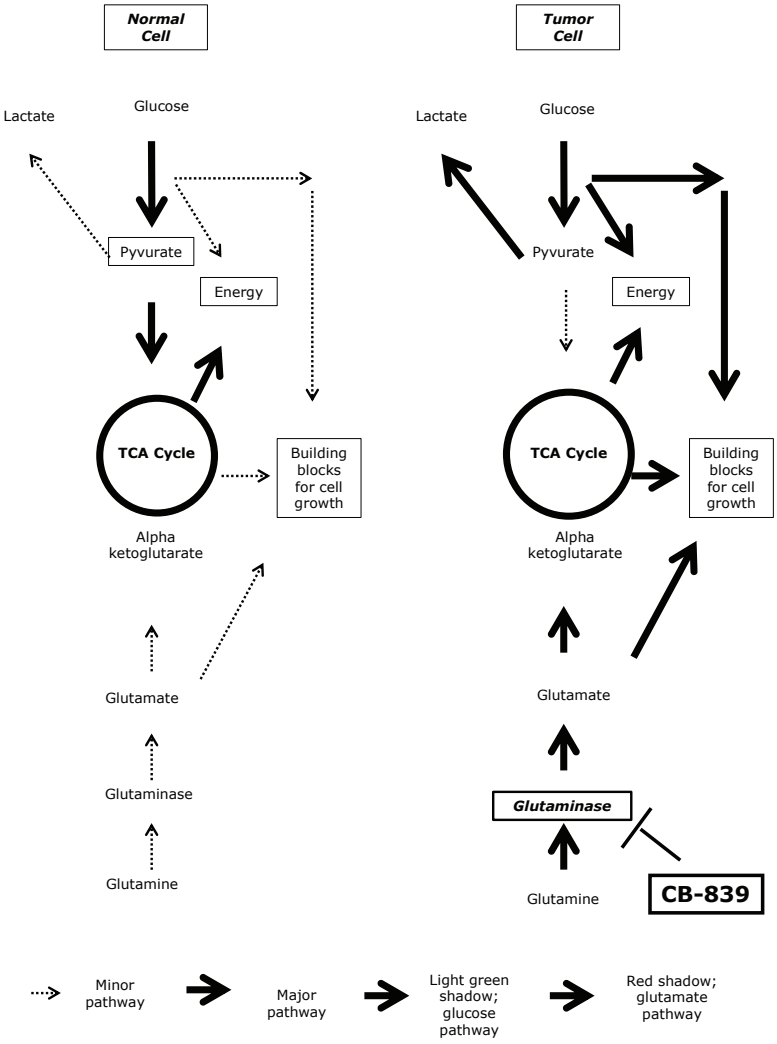
Cell growth, and if the cells enter the cell cycle, it is duplicated via cell division.

Note: rectangles represent glucose, triangles are amino acids, circle is nucleus, star is growth factor, and black explosions are mitochondria.

Source: Adapted from Mendelsohn et al. 2008 *The Molecular Basis of Cancer*, and Wells Fargo Securities, LLC

Tumor cells are more reliant on glutamine as their primary source for energy and building blocks for macromolecules to support cell growth and survival. In a normal cell, glucose is converted to pyruvate through glycolysis in the cytoplasm and subsequently enters the mitochondria and then the TCA cycle, where it is utilized in the creation of energy and biomass macro molecules (see Exhibit 9). In contrast, in the cancer cell, which has undergone/is undergoing a metabolic transformation, due to myriad genetic mutations, its glucose demands are significantly increased. However, much of the glucose taken up into the cell does not enter the mitochondria and, instead, is excreted as lactate (after conversion from pyruvate). As noted in Exhibit 9 in the left-hand panel, glutamine has a secondary role in the normal cell, but in the cancer cell it becomes a primary contributor to creation of energy and macromolecules (refer to the illustration on the right side). Glutamine is converted to glutamate by a mitochondrial enzyme, glutaminase. Glutamate in then metabolized to α-ketoglutarate (the anion of α-ketoglutaric acid), which is a key TCA cycle intermediate. α-ketoglutarate is then further metabolized through the TCA cycle, where it contributes to ATP formation and ultimately, to (oxaloacetate and) citrate creation, which is utilized for fatty acid and cholesterol biosynthesis. This process is known a glutaminolysis. As noted in the lower right-hand corner of the following exhibit, CB-839's mechanism of action is to bind/antagonize glutaminase so that it does not convert glutamine to glutamate. By binding glutaminase, the lower levels of glutamate may contribute to cancer cell death due to lower quantities being available for energy formation and creation of biomass macromolecules.

Exhibit. 9. Glucose and Glutamine Pathways



Source: Adapted from Calithera corporate presentation dated August 6, 2014, and Wells Fargo Securities, LLC

Cancer cells have a truncated TCA/Krebs cycle, making glutaminase inhibition an attractive cancer target. In a normal cell, through glycolysis glucose is converted into pyruvate in the cytoplasm, whereupon it enters the mitochondria and then begins the eight-step biochemical process called the TCA/Krebs cycle (see Exhibit 10).

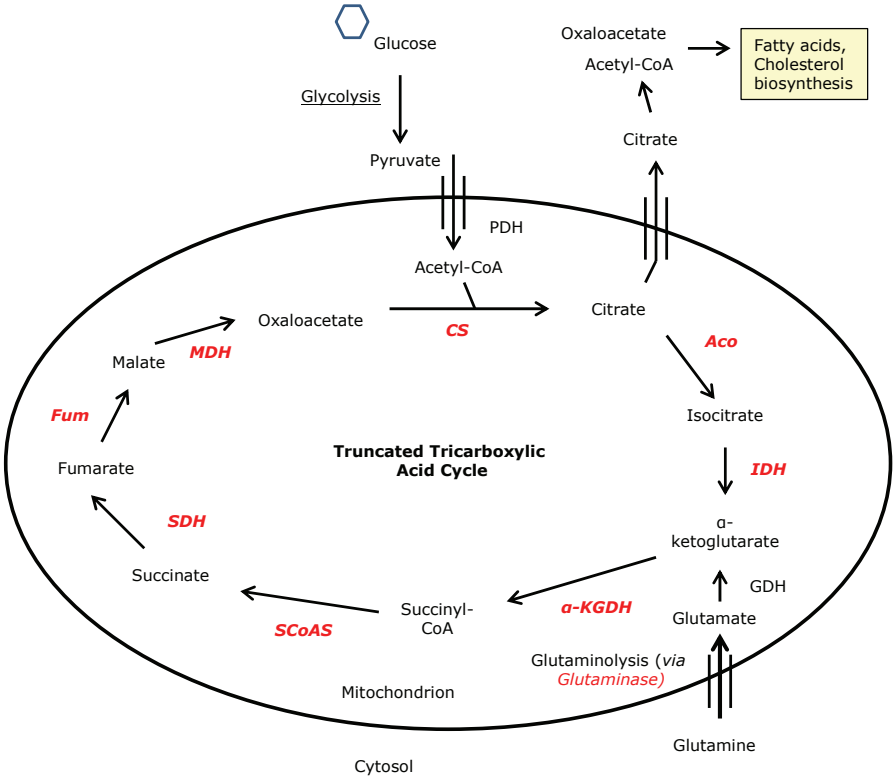
- After entering the mitochondria, pyruvate is converted into Acetyl-CoA via an enzyme called pyruvate dehydrogenase (PDH) and then condenses with oxaloacetic acid (OAA) to form citrate.
- There are eight enzymes involved in the TCA cycle: (1) Aco: aconitase; (2) IDH: isocitrate dehydrogenase; (3) α-KGDH: alpha ketoglutarate dehydrogenase; (4) SCoAS: Succinyl-CoA synthetase; (5) SDH: succinic dehydrogenase; (6) Fum: fumarase; (7) MDH: malate dehydrogenase; and (8) CS: citrate synthase.
- In cancer cells, though, instead of Acetyl-CoA cycling around the TCA to oxaloacetic acid to create energy (as represented below), Acetyl-CoA is converted to citrate by citrate synthase, and a significant portion of citrate is then "shunted" out of the TCA and is used to create fatty acids and cholesterol in the cytoplasm.
- While TCA cycling is suppressed during tumor growth, most tumor cells retain the capacity for traditional TCA activity, though at a diminished rate from non-proliferating cells.

- Efflux of citrate out of the TCA creates a problem for the TCA cycle as there is now less citrate available to continue the Kreb's cycle and generate the energy and replenish the TCA cycle intermediates needed to create biomass macromolecules.

- It is as this point that the glutamine pathway becomes critical to the cancer cell. As noted in Exhibit 10, glutamine enters the mitochondria, is converted by glutaminase to glutamate, and glutamate is subsequently converted to α-ketoglutarate by glutamate dehydrogenase (GDH). As a result, α-ketoglutarate is replenished and then continues the "truncated" Kreb's cycle through six additional biochemical reactions, where it creates energy and ultimately creates oxaloacetate, which is then converted to citrate and eventually shunted out of the mitochondria to create fatty acids and cholesterol.

- Due to the cancer cell's reliance on glutamine replenishing a key TCA cycle intermediate (α-ketoglutarate), which is critical for creation of energy and the pool of intermediates needed to support biomass molecules, inhibition of glutaminase offers a rationale and attractive target for killing cancer cells.

Exhibit 10. The Truncated TCA/Kreb's Cycle



Source: Adapted from Mendelsohn et al. *The Molecular Basis of Cancer* 2008, page 195 and Wells Fargo Securities, LLC. *Note:* italicized, bold, and red acronyms represent enzymes involved in TCA cycle.

What Is Glutamine? Why Is It Important?

Glutamine metabolism is second only to the Warburg effect in terms of historical significance to the study of tumor cell metabolism. According to DeBerardinis (2008 and 2010) dating back to the 1950s, cancer biologists have long recognized the importance of glutamine as a tumor nutrient. In Greenberg's 1956 paper, "Role of glutamine in protein synthesis by the Ehrlich ascites carcinoma," tumors were observed to consume glutamine at high rates. In tumor cells, glutamine (as a substrate) contributes to virtually every core metabolic task of proliferating tumor cells as it participates in bioenergetics, supports cell defenses against oxidative stress, and complements glucose metabolism in the production of macromolecules (e.g., nucleotide, amino acid, lipids, cholesterol synthesis). Although most tissues can synthesize glutamine, during periods of rapid growth or other stresses, demand outpaces supply and glutamine becomes conditionally essential.

Glutamine is one of 20 amino acids encoded by the standard genetic code, is considered an essential amino acid, and has two major isoforms: glutaminase 1 (GLS1) and GLS2. Two splice variants of GLS1 exist and include codons GAC and KGA. GAC is widely expressed in a number of tumor types, while KGA appears to be present in normal tissues; both are over-expressed in cancers. In human blood, glutamine is one of the most abundant free amino acids with a concentration of 500-900 μmol/L. GLS1 is an important downstream effector of Myc and promotes the entry of glutamine into the TCA cycle, whereas GLS2 is regulated by the tumor suppressor gene p53 and influences the cellular redox state by driving *de novo* synthesis of glutathione. GLS2 is primarily expressed in the liver and is 70% homologous with KGA and GAC. Research suggests that tumors do not appear to express much GLS2.

Glutamate is a precursor of glutathione, a major cellular antioxidant, and reduction of glutathione levels could exacerbate cancer cell death. Glutathione is a major endogenous antioxidant and helps combat oxidative stress. In tumors, maintaining a supply of glutathione is critical for cell survival because it allows cells to resist the oxidative stress associated with rapid metabolism, DNA damaging agents, inflammation, and other sources. As a result, by blocking conversion of glutamine to glutamate, CB-839 may bring about cancer cell apoptosis by (1) decreasing the pool of TCA intermediates needed to generate energy and biomass macromolecules (thus inhibiting cellular survival and growth), and (2) decreasing the pool of glutathione so that cancer cells cannot combat oxidative stress as effectively.

Long-term inhibition of glutaminase remains a key question for CB-839's safety profile. While inhibition of glutaminase in the Ph. I CB-839 studies has not generated a safety signal to date, and most important, no neurotoxicity safety issues have arisen, the long-term effects of inhibiting glutaminase and the resulting lower levels of glutamate remain to be seen. In neuroscience, glutamate is an important neurotransmitter that plays the principal role in neural activation. As we discuss further on in this report, older glutaminase inhibitors were less specific and crossed the BBB and caused significant CNS toxicities. CB-839 is more selective, binds at an allosteric binding site for GLS1, and does not efficiently cross the BBB. As a result, in theory, CB-839 should not have similar deleterious effects on the CNS; however, only long-term studies will ultimately answer this question, in our view. In addition to CNS toxicities, lymphocytes are also dependent on glutamine metabolism, thus, a key adverse event to track in the future is immunosuppression and development of severe infections, etc., in our view. Finally, due to potential compensatory mechanisms whereby cancer cells may be able to address some of their energy needs, in spite of inhibition of glutaminase, development of resistance to CB-839 should be an important issue. We note that to date, pre-clinical and early human data (in 24 patients) have revealed no evidence of immunosuppression, CNS toxicities, or development of resistance to therapy.

CB-839's Ongoing Clinical Development Program

CB-839 is a novel, oral, twice or thrice daily, first-in class glutaminase inhibitor. Unlike previous glutaminase inhibitors, CB-839 does not efficiently cross the BBB, it binds glutaminase (GLS1) at an allosteric binding site, does not inhibit other glutamine-utilizing enzymes, and is more specific; thus, the potential for significant CNS toxicities is lower, in our view. Current Ph. I monotherapy studies are evaluating thrice daily dosing (TID), but due to its 6-8 hour half-life, Calithera may explore twice daily dosing (BID) in Ph. I(b)/II studies. CB-839 is not a Cyp enzyme inhibitor, thus limiting the potential for drug-drug interactions.

Exhibit 11. CB-839 Product Profile to Date

Mechanism:	Oral inhibitor of the glutaminase enzyme with biochemical IC_{50} of 24nM for GLS1 GAC and 29nM for GLS1 KGA. CB-839 does not inhibit GLS2.
	Allosteric binding (as were "compound 986" and BPTES). *No off-target effects to date including neurological which were observed in prior glutaminase inhibitors.*
PK profile:	6-8 hours 1/2 life; slowly reversible kinetics; non-covalent.
Dosing:	TID in Ph. I(a); potentially BID in the future. 21-day dosing cycles.
Dose range:	Started at 100mg TID.
	As of 7/25/14: up to 400mg in -001, up to 250mg in -002, and up to 600mg in -003 study. Dose escalation continues.
	Maximal inhibition expected at 400mg to 800mg (irrespective of solid or blood cancer).
	CALA doesn't believe a maximum tolerated dose will be reached.
	Drug concentration has increased with dose.
Dosing goal/schedule:	Achieve continuous (24-hour) 90%+ inhibition of glutaminase.
	Preclinical PK data suggest 300nM in plasma serum at trough level for 24 hours is appropriate target for 90%+ inhibition.
Efficacy:	***4 cases of disease stabilization.*** Mesothelioma and two myeloma patients responded for five cycles. Triple negative breast cancer patient still responding after three cycles (***13% tumor shrinkage***).
Safety*:	Grade 1: 21 cases
	Grade 2: 2 total cases
	Grade 3: 2 total cases
	No reported cases of neurological toxicities.
Biomarker Strategy:	All Ph. I patients will have glutaminase levels assessed by platelet assay. TNBC patients will have biopsies, as well.
Impact on GLS1 and 2 enzymes?	Does not affect GLS2 in liver and does not efficiently cross the blood-brain-barrier, so it does not inhibit GLS1 (GAC or KGA) in the brain, thus a decreased potential for CNS toxicity.
Key unknown safety issues:	1) Will resistance develop in humans? If so, how is this overcome? What are its effects? What are long-term impacts of continuous inhibition of glutaminase, if any? 2) Immunosuppression? 3) CNS toxicity?

Source: Company reports and Wells Fargo Securities, LLC

Note: *= as of July 25, 2014 in 24 patients.

Ph. I program overview. Calithera initiated three Ph. I monotherapy, dose-escalation studies in early 2014. The three studies include (1) solid tumors, (2) MM/NHL, and (3) ALL/AML. In addition, the solid tumor study is to include patients that have rare cancers characterized by TCA cycle enzyme driver mutations. The three studies include adaptive design elements that allow Calithera and investigators to increase or decrease the size of the studies based on the efficacy and safety observed. The protocols also allow for rapid progression into Ph. I(b) combination studies once a sufficient number of patients has been dosed and Calithera has identified the dose it believes will allow for continuous 90+% inhibition of glutaminase. While the primary goals of the Ph. I studies are to assess safety, identify the go-forward Ph. II dose, confirm glutaminase is the appropriate biomarker to assess CB-839, and identify the most promising patient populations to pursue in future studies, signals of clinical activity have been observed in a heavily pre-treated patient population. To date, four cases of disease stabilization have been observed, while toxicities/adverse events have appeared to be primarily mild. To date no neurological toxicities have been observed and the two cases of Grade 3 toxicities may be attributable to the patients' underlying disease. Calithera expects to identify its go-forward dose by late 2014 and subsequently initiate the Ph. I(b) combination studies in MM and TNBC, while it continues the three broad Ph. I monotherapy studies.

Ongoing Ph. I(a)/(b) studies are designed to identify solid tumors and blood cancers most sensitive to glutaminase inhibition. Calithera initiated the Ph. I program in early 2014 and as of July 25, 2014, had enrolled 24 patients across the three ongoing studies.

- Dosing started at 100mg TID and Calithera is targeting 90+% continuous (e.g., 24 hours) inhibition of glutaminase. CB-839 is dosed in 21-day cycles with no rest/break in between each cycle.
- CX-839-001 is the solid tumor study primarily targeting non-small cell lung cancer, TNBC, colorectal cancer, and rare tumors that are characterized by TCA cycle enzyme driver mutations. A number of investigators in the -001 study treat patients with these rare tumors. If the Ph. I data are promising in these rare tumors, Calithera may have a quicker path to market in the United States and possibly, Europe, compared to its current plans to pursue Ph. II and potentially, Ph. III studies for TNBC and R/R MM.
- CX-839-002 includes MM and NHL patients.
- CX-839-003 is focused on ALL and AML.

The studies are currently in the monotherapy dose-escalation phase, and to date, have recruited patients with advanced disease, as noted by a mean of five prior failed therapies (and some as high as 15). In addition, in the -001 study, patients with less prevalent solid tumors (e.g., mesothelioma) can enter the study. Calithera has indicated that it expects to treat a total of about 130 patients in the ongoing monotherapy and future Ph. I(b) combination studies. We note that information on www.clinicaltrials.gov indicates that the protocols could allow for up to about 265 patients to participate in the studies (if the Ph. I(b) studies recruit up to 30 patients in both studies).

Exhibit 12. Phase I/II CB-839 Clinical Program

Phase I(a)/(b) and II CB-839 clinical program

Study	"N"	Population	Phase I(b) portion of program	Potential Phase II design
CX-839-001	~100	TNBC	CB-839 + paclitaxel (n=10-12 patients)#	TNBC: Randomized: CB-839 + pac vs. pac + placebo (n= ~200-300; TBD)
		NSCLC	TBD	
		Driver mutations*		
CX-839-002	~65	MM	CB-839 + pomalidomide/dexamethasone (n=10-12 patients)#	MM: Randomized: CB-839/pom/dex vs. pom/dex/placebo (n= ~200-300; TBD)
		NHL	TBD	
CX-839-003	~40-50	ALL	TBD	TBD
		AML^		

Source: Company reports, www.clinicaltrials.gov, and Wells Fargo Securities, LLC

Note: *= rare mutations such as GIST and HLRCC and will represent ~10% of recruited patients; ^= can include treatment-naives if 60+ years and are ineligible for transplant or standard chemotherapy. #= depending on activity could increase to 30 patients.

The Ph. I(b) portion of the program is to commence later in 2014, setting the stage for Ph. II in 2016. As of October 2014, Calithera is still in the dose-escalation phase of the monotherapy studies. Once the most safe and efficacious dose is identified, Calithera plans to enroll up to 12 patients each in Ph. I(b) studies of CB-839 plus paclitaxel in TNBC and CB-839 plus Pomalyst/dexamethasone in R/R MM. Calithera may enroll up to 30 patients in both of the Ph. I(b) studies, depending on what efficacy is observed in the studies. The decision to pursue R/R MM and TNBC was driven in part by the pre-clinical data, suggesting CB-839 has synergistic effects with paclitaxel and Pomalyst, respectively. While these two Ph. I(b) studies progress through 2015, the Ph. I(a) monotherapy studies will likely continue to accrue patients, and those that respond to therapy are to continue to be treated with CB-839, helping assess the drug's safety and efficacy profile. In addition, Calithera should be able to identify whether CB-839 may be useful in treating other solid tumor and blood cancers. The two Ph. I(b) studies are expected to conclude later in 2015/early 2016 and should set the stage for initiation of larger randomized Ph. II studies in 2016-17.

At this time we assume Calithera pursues a more traditional Ph. II and subsequent Ph. III development program in TNBC and R/R MM. With only 24 patients dosed as of late July and very preliminary signals of clinical activity ,we believe it is premature to assume Calithera will be able to pursue anything but a traditional Ph. II and III development program for CB-839 as this time. However, we note that in the United States, the FDA has shown flexibility with various drug sponsors related to more rapid paths to market. For example, BioMarin was able to move directly from Ph. I/II (without a randomized Ph. II) into a pivotal randomized Ph. III program in BRCA TNBC with its PARP inhibitor BMN673. In R/R MM, Pomalyst was approved based on a Ph. I/II, two-stage study (MM-002) that initially identified the appropriate Pomalyst dose and then subsequently compared Pomalyst/dexamethasone versus Pomalyst. A subsequent randomized study (MM-007) is to serve as the confirmatory study of MM-002, as it compares Pomalyst/Velcade/dexamethasone versus Velcade/dexamethasone. In addition, Array BioPharma has indicated that the Food and Drug Administration (FDA) suggested that the company include an interim ORR analysis for its Ph. III study of filanesib/carfilzomib versus carfilzomib. The ORR analysis would serve as the basis for initial accelerated approval and the final study results based on PFS would provide full approval. Promising Ph. I(b) data in TNBC and/or R/R MM may allow for Calithera to pursue a quicker path to market. Fortunately, PFS appears to be an acceptable regulatory endpoint both in the United States and Europe, and since TNBC and R/R MM (third Line+) progress very quickly (approximately $\leq$ four months in both cancers), the studies can be completed in about 2-3 years.

Exhibit 13. CB-839 Efficacy and Safety Profile

Baseline characteristics of patients and types of solid tumor blood cancers across the studies		
24 enrolled as of July 25, 2014 with relapsed/refractory disease with mean of 5 priors and some up to 15 prior therapies.		
001 Study	Dosing at 400mg	N=15 (5 colorectal; 5 triple-negative breast; 2 renal cell; 1 each: cholangiocarcinoma, sarcoma, mesothelioma
002 Study	Dosing at 250mg	N=3 (multiple myeloma)
003 Study	Dosing at 600mg	N=6 (5 AML; 1 ALL)
Preliminary safety and efficacy in monotherapy dose-escalation phase		
Efficacy	Mesothelioma (N=1)	Duration: 5 cycles
	Multiple Myeloma (n=2)	Duration: 5 cycles
	TNBC (n=1)	On therapy; 3 cycles
		13% tumor shrinkage
Safety	Grade 1: 21 cases	Most common: nausea, vomiting, and fatigue.
	Grade 2: 2 cases	Anemia; had baseline Grade 1 anemia.
		2nd patient: worsening fatigue.
	Grade 3: 2 cases	Elevated creatinine with baseline diabetic nephropathy and severe proteinuria.*
		Neutropenia; had baseline Grade 2 neutropenia.

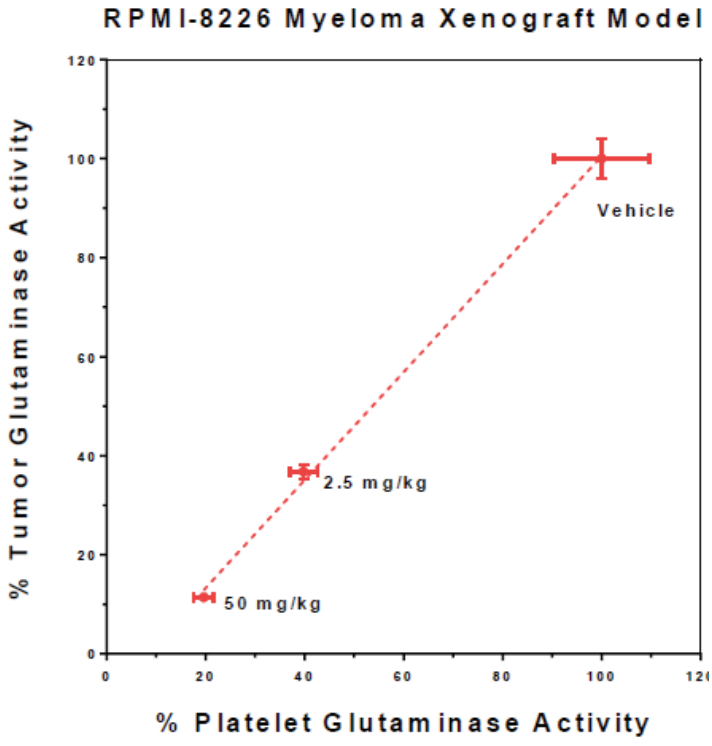
Source: Company reports and Wells Fargo Securities, LLC

Note: * = considered a Dose-limiting toxicity and Serious AE as patient was hospitalized.

Monotherapy data suggest a tolerable drug with initial signals of activity. As noted in Exhibit 13, 24 patients have been enrolled in the three Ph. I studies. The longest duration of dosing has been five cycles, observed in two myeloma and one mesothelioma patient. Tumor shrinkage has been observed in a TNBC patient after only three cycles of CB-839. Dose-escalation continues in all three studies. Due to the advanced stages of disease for patients enrolled in the study to date and the lower doses being assessed in the dose-escalation phase, we see these signals of clinical activity as encouraging. We would expect that as the dose is increased to 400mg+ in -001 and -002 studies, that efficacy should improve. Ideally, at the conclusion of the Ph. I(a) portion in late 2014, an objective response (partial response or even a minor response) will be noted. If so, this could speak well of the potential for improved efficacy in the Ph. I(b) combination studies. Of more importance than efficacy, in our view, is the fact that toxicities appear to be generally mild, with only two Grade 3 (severe) cases observed to date (see Exhibit 13 for details). As part of the standard GLP pre-clinical toxicology package for the IND, Calithera assessed CB-839's effects on rodents' neurological function at very high dose exposures and saw nothing of interest. While the Ph. I studies are still at relatively early stages, the lack of any neurological toxicity to date in humans is a key safety finding as this was the toxicity that halted development of previous glutamines inhibitors.

Ph. I(a)/(b) studies include a biomarker assay. In a pre-clinical study using the RPMI-8226 xenograft mouse model, Calithera demonstrated that the extent of platelet and tumor glutaminase inhibition was directly correlated (see Exhibit 14 for more details). These data, along with the background and development of the pharmacodynamics assay, were presented at the 2014 AACR Meeting (Parlati et al.). As indicated by the exhibit, as the dose was increased, the proportion of glutaminase inhibition in tumor and platelets was generally similar (at dose levels of 2.5mg/kg and 50mg/kg). On the basis of these results, Calithera believes that monitoring glutaminase levels in platelets in peripheral blood can serve as a surrogate for measuring tumor inhibition *in vivo*. The ongoing Ph. I studies are to include the assay to assess all patients' glutaminase levels in platelets, and in the TNBC study expansion cohort (to start in late 2014), Calithera also plans to collect biopsies from TNBC patients, in part to correlate the platelet assay with tumor biopsies and to conduct various gene signature analyses. As noted in the 2014 Gross et al. paper, evaluation of glutaminase activity and the glutamate/glutamine ratio as biomarkers for CB-839 sensitivity in tumor biopsies could be used to select patients with the greatest likelihood to respond to CB-839 treatment. Calithera currently plans to validate the biomarker assay only as part of the Ph. I program and to conduct the assay analyses in its laboratories.

Exhibit 14. Presentation at the 2014 AACR Meeting on the CB-839 novel PD assay.



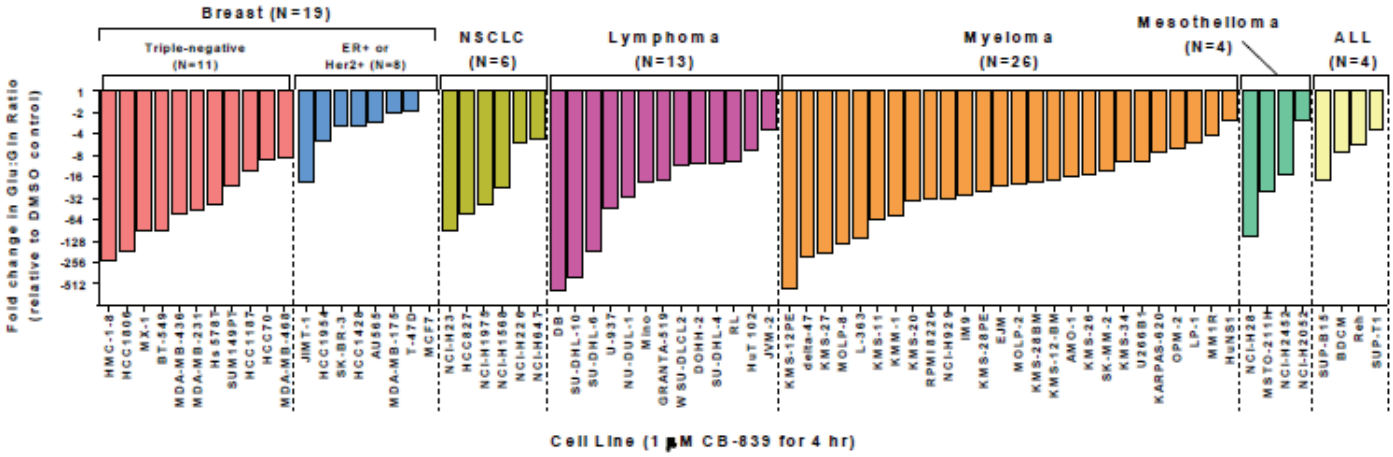
Source: Parlati et al. AACR 2014 Meeting. Reproduced with permission from Calithera.

Extensive Pre-clinical Program Helps Establish Proof-of-Concept of Glutaminase Inhibition

Pre-clinical data have been presented at major medical meetings during 2013 and 2014, and published in a peer-reviewed journal. Pre-clinical data in cancer cell lines and animal models have been presented at the 2013 American Association for Cancer Research, American Society of Hematology, San Antonio Breast Cancer Symposium, and the 2014 American Association for Cancer Research Meetings (which included an oral presentation on Calithera's novel pharmacodynamics biomarker assay). In addition, pre-clinical data in TNBC and Estrogen Receptor positive models were published in *Molecular Cancer Therapeutics* 2014:13; 890-901, Gross et al., "Antitumor activity of the Glutaminase Inhibitor CB-839 in Triple-Negative Breast Cancer." In the following paragraphs we highlight a number of key data that helped establish early proof-of-concept that inhibition of glutaminase with CB-839 correlates with increases in cellular glutamine and decreases in important TCA cycle intermediates (e.g., glutamate, malate), which ultimately appears to contribute to cancer cell death in a broad range of cancers.

Calithera's "A-ha!" moment, which showed CB-839's potential for broad solid tumor and blood cancer activity. Seventy-two cell lines were treated with 1μM of CB-839 for 4 hours to assess glutamine and glutamate ratios/levels and in a separate experiment, 100 different cell lines were exposed to a range of concentrations of CB-839 for 72 hours in order to assess CB-839's anti-proliferative effects. As noted in the following exhibit, CB-839 treatment resulted in varying levels of glutamate/glutamine ratio changes, helping to demonstrate the differing degrees of sensitivity of glutaminase inhibition and the importance of glutamate to those respective cell lines. CB-839 treatment resulted in increased tumor glutamine concentrations and reduced glutamate and aspartate concentrations, confirming glutaminase inhibition in the tumors.

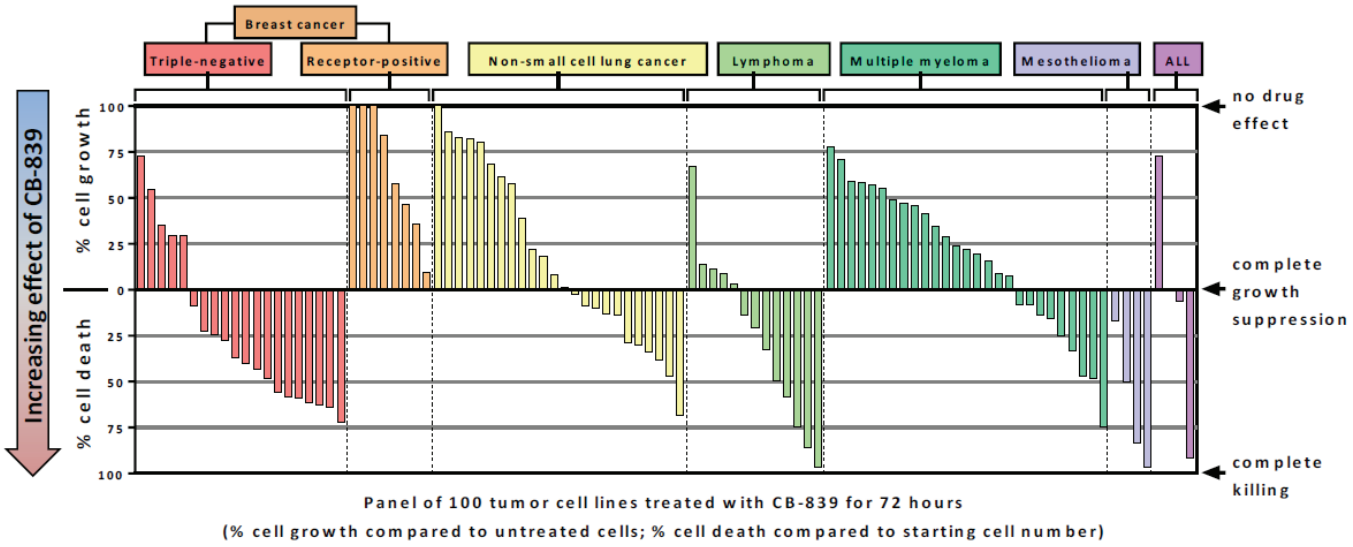
Exhibit 15. CB-839 Is Active In Multiple Solid Tumors And Blood Cancers



Source: Parlati et al. 2014 AACR Meeting. Reproduced with permission from Calithera.

In addition, the changes in levels of glutamate/glutamine correlated with the level of efficacy observed with CB-839. As noted in Exhibit 16, "Pre-clinical Activity of CB-839 in Solid Tumor and Hematologic Cancer Cell Lines," CB-839 treatment resulted in varying degrees of tumor killing and also showed that a majority of cell lines that were tested were sensitive to inhibition of glutaminase. Efficacy ranged from tumor death to growth suppression, to limited or no drug effect. In addition to helping establish a link between inhibition of glutaminase and tumors' dependence on glutamate, these data also indicated the broad activity of CB-839 across multiple tumor types and blood cancers and have helped guide Calithera's broad Ph. I plan looking at CB-839's potential efficacy in TNBC, NSCLC, other solid tumors, leukemias, lymphomas, and MM.

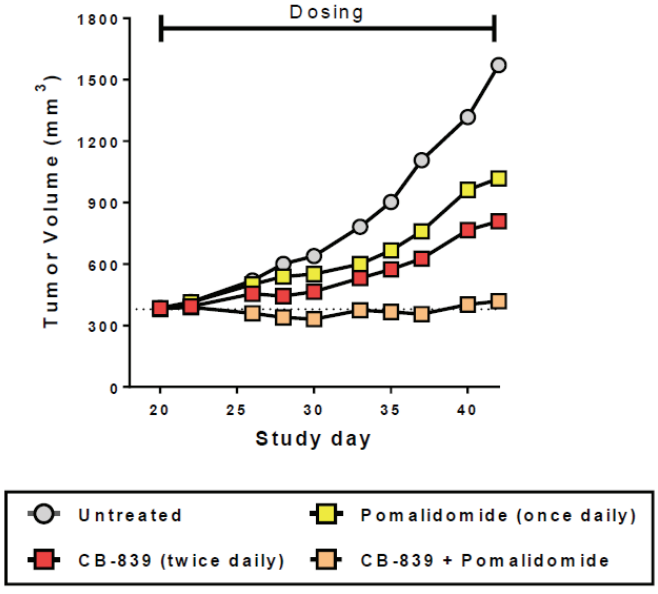
Exhibit 16. Pre-clinical Activity of CB-839 in Solid Tumor and Hematologic Cancer Cell Lines



Source: Calithera company presentation dated August 6, 2014. Reproduced with permission from Calithera.

ASH 2013: Out of 44 MM, NHL, and ALL cell lines treated with CB-839, 41 lines demonstrated a 70% reduction in growth and 11 lines demonstrated cell death. In the MM RPMI-8226 model, a 71% reduction in tumor volume was observed, while there were no apparent deleterious effects on hematologic cell counts (e.g., no cytopenias) or body weight of the mice. Following the early proof-of-concept data in blood cancer cell lines, Calithera conducted an experiment with CB-839 monotherapy (dosed BID), Pomalyst (dosed QD), vehicle/untreated, and CB-839/Pomalyst. After 45 days of dosing CB-839 demonstrated better tumor suppression than Pomalyst, while the combination of the two resulted in minimal tumor volume growth (see following exhibit).

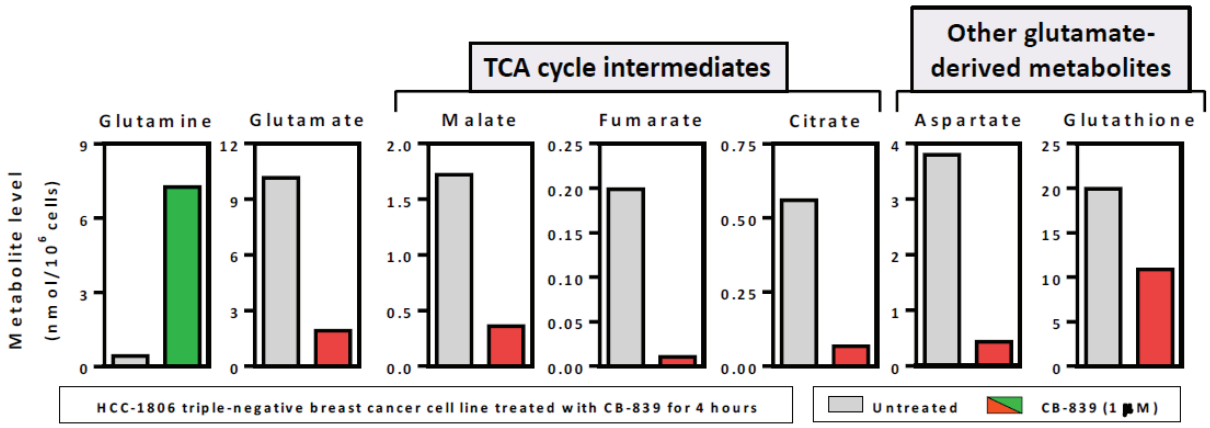
Exhibit 17. Combination of CB-839/Pomalyst Demonstrates Good Tumor Growth Control



Source: Calithera company presentation dated August 6, 2014. Reproduced with permission from Calithera.

SABCS 2013, AACR 2014, Keystone Symposium on Cancer Metabolism, and Gross et al. publication: various data from pre-clinical studies in Triple-Negative and Estrogen Receptor positive breast cancers (and other solid tumors) were presented and published. CB-839 was tested for 72 hours in two TNBC (HCC1806 and MDA-MB-231) and one ER positive (T47D) cell lines to assess these lines' relative sensitivity to glutaminase inhibition. As depicted in the following exhibit, the HCC1806 cells lines demonstrated a significant increase in intra-cellular glutamine levels, a decrease in glutamate, and reductions in TCA cycle intermediates, malate, fumarate, and citrate. In addition, aspartate, and glutathione levels also decreased. As expected, and consistent with other literature (Kung et al. 2011), CB-839 had minimal effect on glutamine consumption in the ER+ T47D cell line. As noted in the Gross et al. paper, the differential effects of CB-839 on glutathione levels in the HCC1806 cell lines were particularly striking. Due to glutathione's role in managing cellular redox, a decrease in glutathione levels puts the cancer cell under additional stress as reactive oxygenated species (ROS) increase. As a result, the cancer cell has a higher likelihood of apoptosis due to lower energy, fewer macromolecules (to support cell growth), and elevated cellular stress due to higher levels of ROS.

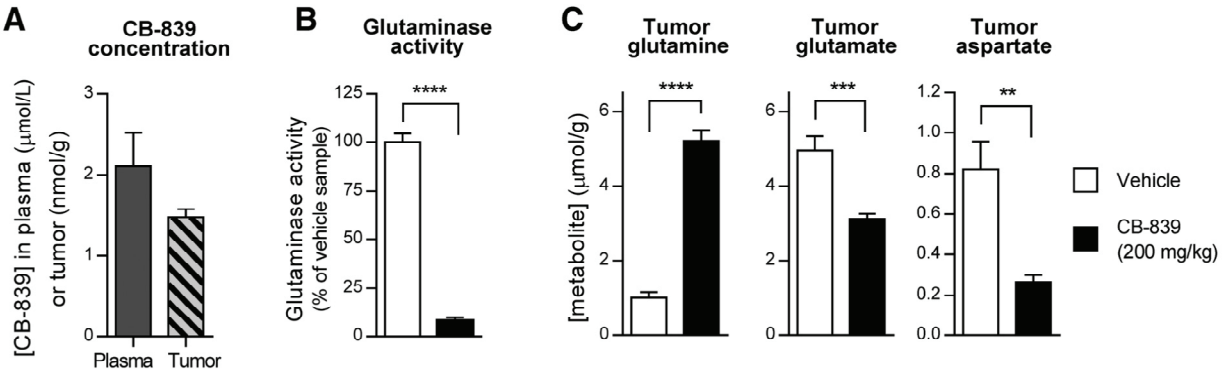
Exhibit 18. *In vitro* HCC-1806 TNBC Proof Of Concept



Source: Calithera presentation dated August 6, 2014. Reproduced with permission from Calithera.

These important TNBC cell line data were re-enforced by results from murine models. CB-839's anti-tumor activity was assessed in a mouse model bearing HCC1806 tumors. In Panel A, CB-839's (PK profile) concentration in plasma and tumor are noted. Panel B highlights the pharmacodynamic effects of CB-839 with a marked and significant decrease in glutaminase level activity. Panel C highlights the significant increases in glutamine levels in the tumor, while glutamate and aspartate were significantly reduced (consistent with the *in vitro* cell data presented above).

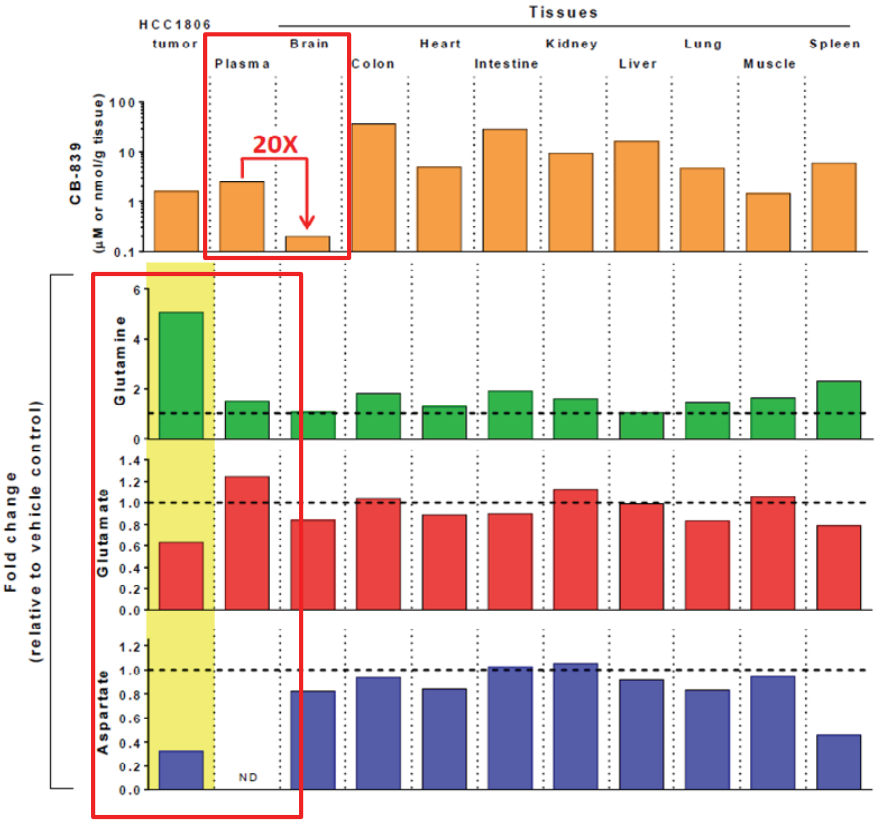
Exhibit19. Pre-Clinical *In Vivo* Breast Cancer Data Establishes Proof-Of-Concept



Source: Gross et al. *Mol Cancer Ther* 2014 page 899. Reproduced with permission from Calithera.

- The top row of Exhibit 20 (see below) illustrates the broad distribution of CB-839 across multiple tumor tissue types, including very low levels in the brain, suggesting the drug does not efficiently cross the BBB.
- With the exception of the brain and liver -- where CB-839 does not effectively cross the BBB and in the liver where GLS2 is expressed and not affected by CB-839 -- glutamine levels increased in all other tissues (see second panel from the top in the following exhibit). Glutamine levels were greatest in the tumor (far left column). Note: the dotted lines represent normal levels or no change.
- Glutamate and aspartate levels were only meaningfully reduced in the HCC 1806 tumor, lung, and spleen (bottom two rows of the following exhibit).
- The authors concluded that these pharmacodynamics data suggest CB-839's effect is largely tumor selective.

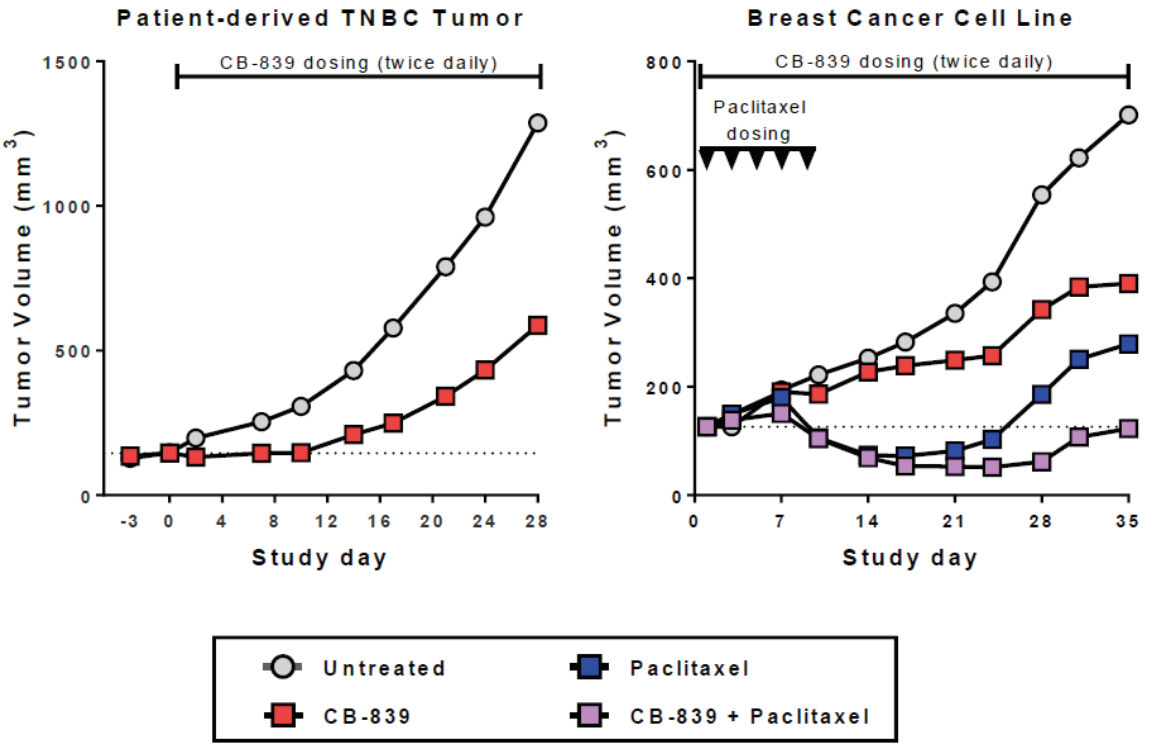
Exhibit 20. *In Vivo* Pre-Clinical Data Confirm *In Vitro* Cell Culture Proof-Of-Concept Data



Source: Calithera company presentation dated August 6, 2014, and AACR 2013 Meeting. Reproduced with permission from Calithera.

In addition to these pre-clinical data from the HCC1806 model, CB-839 demonstrated efficacy as a single agent and in combination with paclitaxel in two xenograft models. Calithera tested CB-839 in two xenograft models: (1) a patient-derived TNBC xenograft and (2) a cell line-based xenograft model using HER2+ basal-like cell line JIMT-1. Single agent CB-839 in the patient-derived model suppressed tumor growth by 61%, compared to vehicle control (p=0.0029), while in the JIMT-1 model CB-839 monotherapy was less effective than paclitaxel in suppressing growth (54% versus 73%) as compared to control. In combination, no growth in tumor volume was observed after 35 days.

Exhibit 21. Single Agent And Combination Efficacy In Xenograft Models



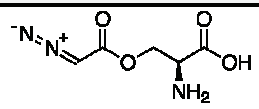
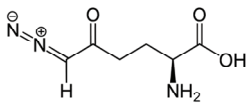
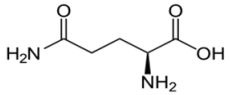
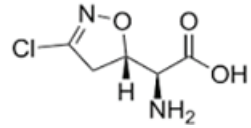
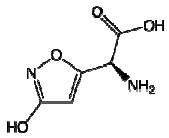
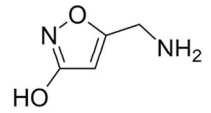
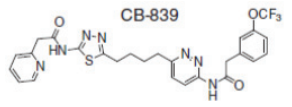
Source for both graphs: Calithera company presentation dated August 6, 2014. Reproduced with permission from Calithera.

Prior Glutaminase Inhibitors

Neurotoxicity was a key safety hurdle, which halted development of prior glutaminase inhibitors. While CB-839 has only generated four cases of disease stabilization as of July 25, this can be attributed, in part, to the low starting dose in the studies, the advanced nature of patients' disease, and limited number of patients dosed. Perhaps more important from the early monotherapy data is the fact that no cases of neurotoxicity have been reported to date. As noted in the following exhibit, a number of other glutaminase inhibitors have been studied in human clinical trials, including azaserine (1954), DON (last reported data in 2008), and acivicin (1984-1998). Limited efficacy was reported in 11 studies, with a partial response occurring in a study combining DON with pegylated glutaminase. In a large number of the studies no objective responses occurred. This lack of objective responses is in large part due to these compounds' narrow therapeutic windows, having less selectivity than CB-839 for glutaminase, crossing the BBB, and irreversible binding characteristics. With the exception of DON with pegylated glutaminase, all other monotherapy compounds developed rapid onset of clinically significant CNS toxicities, such as lethargy, confusion, nightmares, and hallucinations. In addition to CNS toxicities, a number of studies reported moderate/severe cytopenias. As noted by McGovren in 1985 the mechanism for CNS toxicity associated with acivicin was not well understood. The author noted similarities between acivicin's chemical structure, and that of glutamine and those of ibotenic acid and muscimol (the latter being a potent agonist of GABA A receptors and known for inducing sedative-hypnotic and dissassociative psychoactivity). *Note:* we provide the chemical structures for these various compounds, glutamine, and CB-839 in Exhibit 22 for illustrative purposes.

Due to its allosteric binding site properties and less efficient crossing to the blood-brain-barrier, CB-839 appears to avoid neurotoxic effects of prior inhibitors. While GLS1 is present in the brain, CB-839 does not efficiently cross the BBB, and as a result, does not appear to share similar CNS side effects like older glutaminase inhibitors. As of July 25, 2014, Calithera's S-1 does not mention any Grade 1-3 CNS toxicities. While median time on drug and follow-up is limited and CB-839 is still in the dose-escalation phase, the lack of any CNS toxicity to date is encouraging because it developed very rapidly in the afore-mentioned glutaminase inhibitor studies.

Exhibit 22. Prior Glutaminase Inhibitors

Compound	Mechanism of Action	Year, Publication	"N", cancers	Efficacy	Toxicities	Chemical Structure
Azaserine	Competitive inhibitor of glutamine amidotransferase	1954	N=89 adults/children; solid tumors and blood cancers	Transient responses in Hodgkin's, CLL, and pediatric acute leukemia	CNS (apathy, confusion), GI, leukopenia and thrombocytopenia, systemic intoxication with or without liver damage.	
DON (6-Diazo-5-oxo-L-norleucine)	Mitochondrial glutamine antagonist; exact MOA unclear.	2008 combination with Pegylated glutaminase	N=55 solid tumors	1 PR and 1 prolonged SD	Grade 3/4 fatigue, nausea, vomiting; limited Grade 3/4 neutropenia, thrombocytopenia.	
		None reported since 2008				
Glutamine	*(chemical structure being provided for comparative purposes)*					
Acivicin	Irreversible inhibitor of L-glutamine amidotransferases	O'Dwyer 1984	5 Ph. I's. (1981-1983); 2 Ph. II's (colorectal N=16; breast N=22)	No responses	Ph. I: dose-limited CNS (lethargy, confusion, nightmares, hallucinations). Ph. II: CNS, GI, leukopenia.	
		McGovren 1985	N=12 (solid tumors); two dosing schedules	No responses; 1 stable disease	Mild to moderate CNS (similar to prior Ph. I/II's)	
		Hidalgo 1998	Ph. I acivicin + aminosyn, N=22 solid tumors	Not reported; median 2 cycles.	CNS (2 cases Grade 3/4; 50% had reversible CNS effects during 1st course), Grade 3/4 neutropenia, thrombocytopenia.	
Mechanisms of CNS toxicity for acivicin are not fully understood. The McGovren paper notes that acivicin's structure is similar to ibotenic acid and muscimol, which are known to cause CNS effects similar to those reported for acivicin. Acivicin or a metabolite could have caused the CNS toxicity directly. *Both ibotenic acid and muscimol chemical structures provided for comparative purposes below.*						
Ibotenic Acid	A powerful neurotoxin which is used as a brain lesioning agent.			Muscimol	Potent, selective agonist for GABA A receptors; displays sedative-hypnotic and dissociative psychoactivity.	
CB-839	Mitochondrial glutaminase inhibitor (allosteric binding)	2014 (Calithera S-1)	Ph. I monotherapy; N=24; solid tumors and multiple myeloma	4 cases of stable disease (2 in MM and 2 in solid tumors)	***No CNS toxicities to date***; 2 cases Grade 2 (anemia, worsening fatigue) and 2 cases Grade 3 (neutropenia, elevated creatinine)	
Compound 968 and BPTES are both allosteric inhibitors of glutamine and are in preclinical development with last reported publications in 2013.						

Sources: Company reports, cited publications, Wikipedia (for chemical structures), and Wells Fargo Securities, LLC

Other Oncology Companies Targeting Cancer Cell Metabolism

Currently there are no companies developing glutaminase inhibitors. At this time we are unaware of any other company developing a glutaminase inhibitor for the treatment of solid tumors/blood cancers. A number of companies are targeting cancer cell metabolism, and the respective targets are noted in the following exhibit. We have included Threshold Pharmaceuticals in the list, even though its lead drug targets hypoxia (low oxygen state) and not a metabolic enzyme. The closest "competitor" could be considered Agios, as its oral, small-molecule AG-221 targets the mutated IDH2 protein which is found in the mitochondria and is associated with the Kreb's cycle (see Exhibits 10 and 25). Agios has reported positive Ph. I/II data for AG-221 in AML patients who have mutated IDH2. Agios' science indicates it is more of an epigenetic approach, as opposed to targeting cancer cell metabolism directly. By comparison, Calithera is broadly targeting blood cancers and solid tumors and CB-839 does not directly target the mutated enzyme, IDH2, rather Calithera's CB-839 seeks to shut off the fuel (glutamate), which is important for IDH2 mutated cancers, such as AML and glioblastoma.

Exhibit 23. Selected Oncology Companies Focused on Cancer Cell Metabolism

Company	Metabolism Target	Compound	Status
3V Biosciences	Fatty acid synthesis inhibitor	TVB-2640	Ph. I started late 2013
Advanced Cancer Therapeutics	Glycolysis inhibitor; PFKFB3 inhibitor	PFK-158	Ph. I started May 2014
Cornerstone/Chiesi U.S.A.	PDH and α-KG mitochondrial enzyme metabolism inhibitors	CPI-613	Ph. I efficacy data in hematologic cancers at ASCO 2013; combination AML data at ASCO 2014
Threshold Pharmaceuticals	Hypoxia targeted therapy	TH-302	Ph. I - III multiple solid tumors/hematologic cancers
Eleison Pharmaceuticals	Glucose-conjugated prodrug of isophosphoramide mustard	Glufosfamide	Ph. III pancreatic cancer
Forma Therapeutic Holdings/Roche	NAMPT enzyme inhibitor	Undisclosed	Unknown; agreement announced in 2011; no reported progress
Myrexis	NAMPT enzyme inhibitor	MPC-8640	Ph. I 2011 EORTC data; no longer focused on oncology; complete liquidation in 2012.
Fujisawa GmbH	NAMPT enzyme inhibitor	FK866	2008 Ph. I/II data published; no objective responses; DLT was thrombocytopenia
Agios Therapeutics	IDH2 mutated protein inhibitor (part of the TCA cycle); Epigenetics	AG-221	2014 AACR Meeting, Ph. I/II data in AML; partnered with Celgene

Source: Company reports and Wells Fargo Securities, LLC

Life-cycle management for CB-839

Life-cycle management strategy for CB-839 includes rare cancers associated with TCA cycle enzymes and in combination with oncology therapies that target signaling pathways. While the near-term focus is to advance CB-839 into Ph. II studies as monotherapy and/or in combination with paclitaxel in TNBC and with Pomalyst/dexamethasone in R/R MM in order to capitalize on the apparent link between genetic mutations and increased reliance on glutamine for creation of energy and biomass macromolecules, over the long term, Calithera plans to assess CB-839 with erlotinib (to target EGFR mutations), sorafenib, and trametinib (to target Ras/Raf mutations), and/or MK-2206 or everolimus (to target PI3K/mTOR). Calithera is currently generating pre-clinical data for various CB-839 combinations and is in the early stages of designing studies. The following exhibit highlights various mutations that are believed to be linked to cancer cells' aberrant energy requirements and which drive increased reliance on glutamine/glutamate as a primary fuel source. Highlighting the complex inter-relationships between genetic mutations, low oxygen (hypoxia), and re-wired cancer cell metabolism (tied to genetic mutations), it is worth noting that loss of function by tumor suppressor genes, such as p53, are also believed to play an important role in cancer cell metabolism.

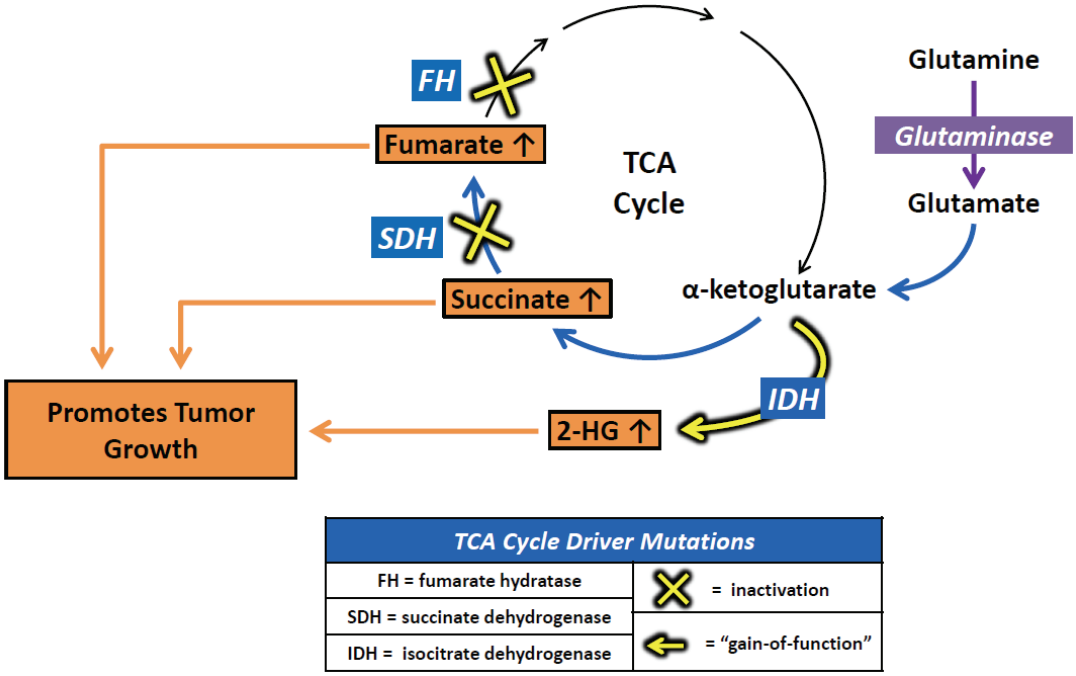
Exhibit 24. Genetic Mutations Underlying Cell Metabolism Shift to Glycolysis and an Increased Reliance on Glutamate

PI3K activates downstream AKT which stimulates glycolysis by directly regulating glycolytic enzymes and activation of mTOR. Constitutively activated signalling of PI3K results in a requirement for nutrient acquisition and utilization.
mTOR enhances hypoxia-inducible factor 1 (**HIF-1α**) which can lead to expression of glucose transporters and glycolytic enzymes and pyvurate dehydyrogenase kinase which blocks entry of pyvurate into the TCA (Krebs cycle).
HIF-1α (tumor hypoxia) facilitates metabolic adaptions, allowing cells to survive and build new vascular supply.
MYC cooperates with **HIF-1α** in activating several genes that encode glycolytic proteins, increase mitochondrial metabolism, increase the number of glucose transporters, and induces expression of enzymes involved in nucleotide metabolism.
RAS proto-oncogenes (e.g., NRAS, HRAS, and KRAS) and mutations can lead to enhanced glucose transport and may enhance mitochondrial metabolism.
p53 opposes the glycolytic phenotype. Loss of p53 results in enhanced glucose transport.
AMPK (AMP-activated protein kinase)-LKB1 (liver kinase B1) tumor suppressor gene opposes the glycolytic phenotype by inhibiting mTOR.

Source: Cairns 2011, DeBerardinis 2008, Vander Heiden 2011, and Wells Fargo Securities, LLC

Ongoing Ph. I studies are to assess CB-839 as a potential treatment option in patients who possess rare tumors with TCA cycle enzyme driver mutations. Approximately 10-15% of the patients in the solid tumor CX-839-001 study will be patients who have TCA cycle enzyme driver mutations. Calithera has included these patients in the study in an attempt to determine whether patients with these rare tumors respond to CB-839. As noted in the following exhibit, there are a number of genes that exhibit loss or gain of function mutations associated with tumors driven by the TCA cycle. As discussed by DeBerardinis (2008), Cairns (2011), and Vander Heiden (2011) mutations that cause inactivation of fumarate hydratase and succinate dehydrogenase lead to increases in the TCA cycle's succinate and fumarate, which, as previously discussed, helps support energy generation and creation of various biomass macromolecules helping cancer cells grow. In addition, a gain of function somatic mutation related to isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2, respectively) leads to conversion of α-ketoglutarate to D-2-hydroxyglutarate (2HG), an oncometabolite found in low quantities in normal cells, but in elevated quantities in cancer cells. Similar to increases in quantities of fumarate and succinate, 2-HG levels increase to high levels in glioma patients and in leukemia, and ostensibly lead to tumor growth (primarily due to epigenetic changes). These mutations have been associated with hereditary leiomyomatosis and renal cell cancer (HLRCC), paraganglioma, pheochromocytoma, chondrosarcoma, cholangiocarcinoma, glioblastoma, and AML. Unlike Agios' small-molecule AG-221, which targets the IDH2 mutated enzyme, Calithera's approach attempts to starve the cancer cell of the fuel, glutamate, which contributes to increasing the levels of α-ketoglutarate and ultimately contributes to elevated levels of 2-HG.

Exhibit 25. TCA Cycle Driver Mutations



Source: Calithera company presentation dated August 6, 2014. Reproduced with permission from Calithera.

At this time we do not include CB-839 estimates for tumors with these rare TCA cycle enzyme mutations. The prevalence for many of these rare driver mutations is not well defined but is estimated to range from a few hundred to a few thousand patients, depending on the tumor type. If Ph. I studies suggest CB-839 is safe and generates clinically meaningful response rates, clinical development in a number of these rare tumors would likely offer a quicker path to market that may only require a single-arm study in a small number of patients and could use ORR as the primary endpoint. We would envision this being similar to a clinical program for rare blood cancers, such as Mantle Cell lymphoma, for example. We plan to await proof-of-concept data for CB-839 in these rare driver mutations before determining if any of these mutations should be included in our valuation.

Our CB-839 Assumptions in TNBC and Third Line+ MM

In TNBC we assume patients will receive an average of eight cycles of therapy (6 months) as median PFS in metastatic TNBC is variable and short, and ranges from 4 weeks in third line up to 12 weeks in first line (Kassam et al. *Clinical Breast Cancer* 2009). We assume CB-839/paclitaxel will need to demonstrate 5-6 months PFS versus about 3.5-4.0 months for paclitaxel in Ph. III, suggesting up to a 50% improvement in PFS. We model an annual 5% price increase in the United States, versus an every-other-year 5% decrease in Europe. In Europe we also assume an average of eight cycles, but a starting price that is about 85% of the U.S. price. We currently model Calithera licensing the ex-U.S. rights in TNBC and MM to a partner following Ph. II; and in exchange for equally splitting R&D expenses, Calithera receives a flat 20% royalty. Finally, we assume a 30% probability of success at this time, due to the early nature of the Ph. I monotherapy clinical data.

Exhibit 26. CB-839 Triple-negative Breast Cancer Revenue Build

Triple-Negative Breast Cancer Revenue Build and Epidemiology Estimates

United States	**2014E**	**2022E**	**2023E**	**2024E**	**2025E**
Breast cancer prevalence	234,600	274,871	280,369	285,976	291,696
~13-15% of all breast cancers are Triple Negative	35,190	41,231	42,055	42,896	43,754
Penetration rate	*0%*	*2%*	*5%*	*10%*	*15%*
Total patients on CB-839	0	825	2,103	4,290	6,563
Cycles of therapy (dosed on 21-day cycles)	0	8.0	8.0	8.0	8.0
Price per cycle	$0	$9,000	$9,450	$9,923	$10,419
Probability of success (25%)					
Total CB-839 sales (000s $) in the U.S.	**$0**	**$8,906**	**$47,691**	**$102,154**	**$164,110**
Europe					
Breast cancer prevalence	375,360	439,794	448,590	457,562	466,713
~13-15% of all breast cancers are Triple Negative	56,304	65,969	67,288	68,634	70,007
Penetration rate	*0%*	*0%*	*2%*	*5%*	*10%*
Total patients on CB-839	0	0	1,009	3,432	7,001
Cycles of therapy (dosed on 21-day cycles)	0	0.0	8.0	8.0	8.0
Cost per cycle €	€ 0	€ 5,885	€ 5,885	€ 5,591	€ 5,591
Exchange rate ($/€)	$1.30	$1.30	$1.30	$1.30	$1.30
Price per cycle in U.S. $	$0	$7,651	$7,651	$7,268	$7,268
Probability of success (25%)					
Total CB-839 sales (000s $) in the EU	**$0**	**$0**	**$18,532**	**$59,860**	**$122,114**
Royalty to Calithera on EU sales	**$0**	**$0**	**$3,706**	**$11,972**	**$24,423**
Total Probability-adjusted CB-839 revenues (000s $)	**$0**	**$8,906**	**$66,223**	**$162,013**	**$286,224**

Source: Company reports and Wells Fargo Securities, LLC estimates

In R/R MM we assume patients will receive an average of eight cycles of therapy (six months) at approval growing slowly over time, a dynamic that has become commonplace in MM as physicians better manage toxicities and "healthier" patients start to use therapy (e.g., second Line versus third Line+). In the pivotal Ph. III Pomalyst/dexamethasone versus high-dose dexamethasone study, median PFS was about four months in the active drug arm. Thus we assume Calithera will need to demonstrate about a 25-50% improvement in PFS to be considered clinically meaningful and warrant broad usage. Similar to TNBC, we model an annual 5% price increase in the United States, versus an every-other-year 5% decrease in Europe. In Europe we also assume an average of eight cycles, but a price that is about 85% of the starting U.S. price. Finally, we assume a 30% probability of success at this time, due to the early nature of the Ph. I monotherapy clinical data.

Exhibit 27. CB-839 Multiple Myeloma Revenue Build

Multiple Myeloma Revenue Build and Epidemiology Estimates

United States	2014E	2021E	2022E	2023E	2024E	2025E
Overall population	318,392,774	334,824,035	337,239,582	339,672,557	342,123,084	344,591,290
Total MM Population	69,130	85,188	87,548	89,926	92,321	94,733
Total U.S. patients on salvage therapy (31%)	21,430	26,408	27,140	27,877	28,620	29,367
Penetration	*0%*	*2%*	*6%*	*8%*	*11%*	*14%*
Number of patients on therapy	0	528	1,628	2,230	3,148	4,111
Cycles of therapy (dosed on 21-day cycles)	0	8.0	8.3	8.5	8.8	9.0
Price per cycle	$0	$8,571	$9,000	$9,450	$9,923	$10,419
Probability of success (25%)						
Total CB-839 sales (in 000's $; probability-weighted)	**$0**	**$5,432**	**$36,273**	**$53,741**	**$81,998**	**$115,655**
Total CB-839 sales (in 000's $; 100% probability)	**$0**	**$36,215**	**$120,909**	**$179,138**	**$273,328**	**$385,518**

Europe (Top 10 Countries: Big 5 + Austria, Belgium, Netherlands, Portugal, Sweden)						
Overall population	376,745,037	390,198,852	392,159,652	394,130,306	396,110,862	398,101,370
Total MM Population	94,195	113,031	115,776	118,535	121,307	124,094
Total European patients on salvage therapy (31%)	29,201	35,039	35,890	36,746	37,605	38,469
Penetration	*0%*	*0%*	*2%*	*4%*	*7%*	*10%*
Number of patients on therapy	0	0	718	1,470	2,632	3,847
Cycles of therapy (dosed on 21-day cycles)	0	0	8	8.25	8.5	8.75
Price per cycle in €	€ 0	€ 0	€ 5,885	€ 5,885	€ 5,591	€ 5,591
Exchange rate ($/€)	$1.34	$1.30	$1.30	$1.30	$1.30	$1.30
Price per cycle in U.S. $	$0	$0	$7,651	$7,651	$7,268	$7,268
Probability of success (25%)						
Total CB-839 sales (in 000's $; probability-weighted)	**$0**	**$0**	**$13,180**	**$27,831**	**$48,787**	**$73,393**
Total CB-839 sales (in 000's $; 100% probability)	**$0**	**$0**	**$43,933**	**$92,771**	**$162,622**	**$244,644**
Royalties to Calithera on EU Sales	**$0**	**$0**	**$2,636**	**$5,566**	**$9,757**	**$14,679**

Total Probability-adjusted CB-839 sales (000s $)	**$0**	**$5,432**	**$49,452**	**$81,573**	**$130,785**	**$189,049**

Source: Company reports and Wells Fargo Securities, LLC estimates

Calithera's strategy of combining CB-839 with Pomalyst is a solid one with no competition. As noted in the following exhibit, CB-839 appears to be the only investigational agent that may be developed as a combination therapy with Pomalyst. Management has noted that in addition to pre-clinical synergistic activity with Pomalyst, its rationale for combining the two drugs stems from the possibility that CB-839 may help re-sensitize myeloma cells that have become resistant to Pomalyst. One of the MM cells lines used in pre-clinical studies was fairly resistant to Revlimid/Thalomid/Pomalyst, yet CB-839 had an effect on cell growth. In our view, the end-stage or third Line+ R/R MM market is one where patients will likely cycle through all lines of available therapy as median PFS tends to be short. As a result, it is more of a question of when a patient will use CB-839/Pomalyst/dexamethasone. Other therapies in Ph. II or III development in end-stage MM include Pharmacyclics/Janssen's ibrutinib/carfilzomib (Ph. II) and Array BioPharma's filanesib as single agent (in a potentially pivotal Ph. II single-arm study assessing responses in low AAG patients) and filanesib/carfilzomib (expected to start Ph. III in 2015).

Exhibit 28. Multiple Myeloma Development Landscape

Novel Agent	Mechanism	1st Line		Relapsed/Refractory				
		Velcade	Revlimid	Velcade	Kyprolis	Pomalyst	Revlimid	Single agent
CB-839	Glutaminase inhibitor							TBD
Ibrutinib	BTK inhibitor							
Filanesib	KSP inhibitor			TBD				
Panobinostat	HDAC inhibitor							
Ixazomib	oral Proteasome inhibitor							
Elotuzumab	CS1 mAb							
Daratumumab	CD38 mAb							
Ricolinostat (ACY-1215)	HDAC inhibitor							
ABT-199	Bcl2 inhibitor							
Kyprolis	Proteasome inhibitor							

Source: Company reports, www.clinicaltrials.gov, and Wells Fargo Securities, LLC

Note: cells with yellow shading and dots indicate announced development strategy for the respective novel agent. Chart does not indicate if combination includes dexamethasome or melphalan/prednisone.

Kyprolis U.S. sales over initial three years provides a reasonable comp for CB-839's global sales launch. As noted, our non-probability-weighted U.S. and EU revenue estimate in the third full year of launch (2024) for CB-839 is $436 million. Consensus estimates for 2014 for Kyprolis (currently approved only in the United States in dual-refractory MM) is $332 million (as per FactSet). Our 2024 CB-839 revenue estimate equates to CB-839 treating about 5,700 (about 9%) of our estimate of approximately 66,000 U.S. and EU-10 third Line+ MM patients in 2024 for a median of 8.5 cycles (or about 6.00-6.25 months). Considering the initial three years of Kyprolis is based only on U.S. sales, we believe our CB-839 sales estimate and underlying assumptions (treatment duration, number of patients, etc.) are reasonable.

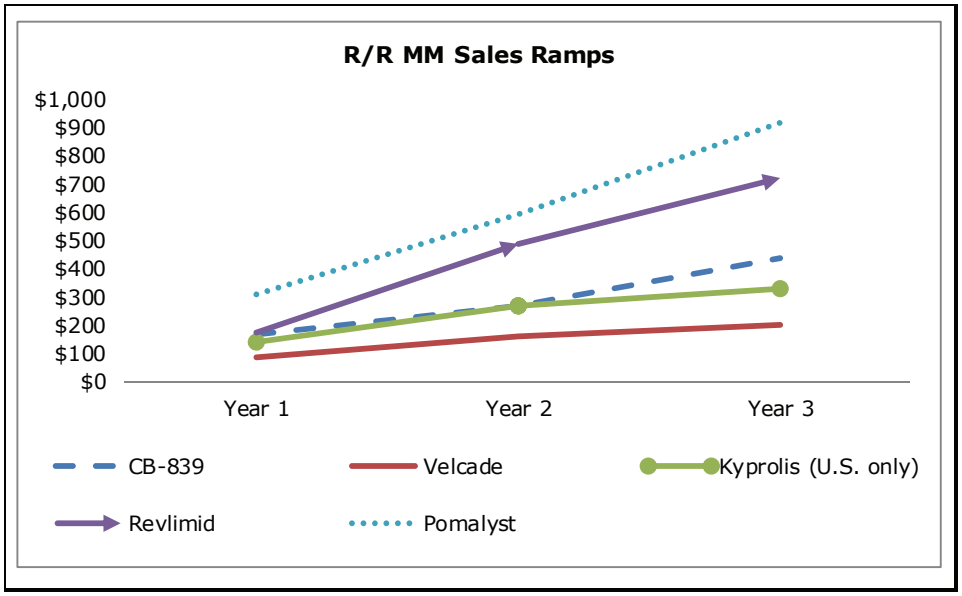
Exhibit 29. CB-893 Estimates versus Other MM Launches

	Year 1	Year 2	Year 3
CB-839	$165	$272	$436
Velcade	$89	$158	$201
Kyprolis (U.S. only)	$141	$267	$332
Revlimid	$172	$485	$725
Pomalyst	$306	$594	$919

Source: Company reports, FactSet, and Wells Fargo Securities, LLC estimates

Note: in $M. Pomalyst is year-to-date for 2014 for Year #2 and annualized off of $297M. Year 3 is based off WFS, LLC estimate of $919M. Kyprolis year 3 is consensus for FY 2014. CB-839: 100% probability-weighted.

Exhibit 30. Wells Fargo estimated CB-839 MM Sales Ramp versus Prior R/R MM Sales Ramps



Source: Company reports, FactSet and Wells Fargo Securities, LLC estimates

Management

Calithera has a solid management team, which helped to develop a future potential block-buster therapy for MM, Kyprolis. Many members of Calithera's management team were previously at private Proteolix through 2009, before the company was acquired by Onyx Pharmaceuticals for up to $841 million in cash (including future success-based milestones). The key clinical stage asset at Proteolix was carfilzomib (Kyprolis), a novel proteasome inhibitor, which was being studied for MM. At the time of the acquisition, Kyprolis was in Ph. II development. Onyx continued the clinical development of Kyprolis, which ultimately led to the successful approval of the drug by the FDA on July 20, 2012, for end-stage myeloma patients who had failed Velcade (Takeda/JNJ's first generation proteasome inhibitor) and an immunomodulatory agent (CELG's Revlimid or Thalomid). Based in part on Kyprolis' clinical profile and the potential for it to be used in first-line myeloma in combination with Revlimid, Amgen acquired Onyx in 2013 for $9.7 billion, net of Onyx's estimated cash.

Development of Kyprolis provides the team with scientific credibility and important regulatory and clinical experiences. CEO Susan Molineaux, Dr. Chris Molineaux, and Dr. Mark Bennett now bring their experiences in developing Kyprolis to Calithera, which we believe are highly leverageable, especially as they relate to prior existing relationships with the FDA, CHMP, and top clinical investigators in the MM field. Although many companies work with many leading clinical investigators, we believe the clinicians participating in the Ph. I CB-839 program include some well-regarded researchers, which should be important in marketing CB-839 if it successfully reaches market. Some of the key clinicians working with Calithera include Keith Stewart, David Siegel, and Jesus Berdeja in MM, Anas Younes in lymphomas, Ian Flinn and Marina Konopleva in leukemias, and Melinda Telli and Jeffrey Infante in solid tumors.

Exhibit 31. Calithera's Senior Executive Team

Executive	Title/Position	Previous Experience
Susan Molineaux, Ph.D.	CEO, President, Founder & Director	Founder and CEO of Proteolix; Rigel, Praecis, Merck
William Waddill	SVP, CFO	SVP, CFO at OncoMed and Ilypsa
Chris Molineaux, Ph.D.	SVP, Development	VP, Development at Proteolix; Fibrogen; J&J; Merck, Mt. Sinai Medical School
Mark Bennett, Ph.D.	SVP, Research	VP, Research at Proteolix
Eric Sjogren, Ph.D.	SVP, Drug Discovery	VP, Medicinal Chemistry at Roche; Syntex

Source: Company reports and Wells Fargo Securities, LLC

Financials

Calithera ended H1 2014 with about $28 million in cash and equivalents. During Q3 2014, it received about $16 million in additional financing from a private Series D offering. As a result of the additional capital, Calithera believed the approximately $44 million in *pro forma* cash was sufficient to fund business operations through the end of 2015, when the Ph. I(b) CB-839 combination studies are expected to conclude. The IPO financing of net $77.4 million is expected to provide sufficient funds to advance CB-839 through the end of Ph. II studies, expected to conclude later in 2017 or early 2018. Calithera has no convertible preferred debt following the October 1, 2014, IPO.

Exhibit 32. Calithera's Balance Sheet

Calithera Biosciences, Inc. Balance Sheet
(In 000's $)

For Period Ended:	*Pro forma* as of 6/30/2014
Assets	
Current assets:	
Cash and cash equivalents	$27,750
Prepaid expenses and other	$1,497
Total current assets	$29,247
Restricted cash	$46
Property and equipment, net	$753
Other assets	$609
Total assets	**$30,655**
Liabilities, Convertible Preferred Stock, and Stockholders' Deficit	
Current liabilities:	
Accounts payable	$1,037
Accrued liabilities	$2,082
Funds received in advance for preferred stock financing	$3,000
Total current liabilities	$6,119
Deferred rent	$297
Total liabilities	**$6,416**
Commitments and Contingencies	
Convertible preferred stock	$0
Stockholders' deficit:	
Common stock	$1
Additional paid in capital	$64,020
Accumulated deficit	($39,782)
Total stockholders' (deficit) equity	$24,239
Total liabilities and stockholders' equity	**$30,655**

Source: Calithera Biosciences, Inc.'s S-1 dated September 25, 2014, and Wells Fargo Securities, LLC

Intellectual Property

In the following exhibit we highlight Calithera's issued CB-839 Composition of Matter patent, which expires in 2032 and multiple U.S. and World patent applications.

We note Elan has been issued patents for inhibition of glutaminase, but these are focused on "Methods of preventing neuronal death" (US 6310093, published 10/30/2001) and "Selective inhibitor of glutaminase by bis-thiadiazoles. Neuroprotection and in the treatment of hepatic encephalopathy" (US 6451828, published 9/17/2002). Takeda's patent US 5552427 A "Glutaminase inhibitory compound, compositions, and methods of use" was granted September 3, 1996, but has lapsed. In addition, Paul A. Rosenberg was granted a patent, "Controlling glutamine/glutamate related neuronal injury," October 27, 1992, but this is not related to oncology/hematology.

At this time it appears Calithera has full freedom to operate, with no competing IP from other companies.

Exhibit 33. CB-839 Patents

Publication Date	Publication Number	Title	Abstract	Estimated expiration	Comments
12/10/2013	US8604016B2	Heterocyclic inhibitors of glutaminase	The invention relates to novel heterocyclic compounds and pharmaceutical preparations thereof. The invention further relates to methods of treatment using the novel heterocyclic compounds of the invention.	2032	Composition of Matter
7/10/2014	US20140194421A1	Heterocyclic glutaminase inhibitors	The invention relates to novel heterocyclic compounds and pharmaceutical preparations thereof. The invention further relates to methods of treatment using the novel heterocyclic compounds of the invention.	2033	Method of treating neurological and immune diseases
2/20/2014	US20140050699A1	Heterocyclic inhibitors of glutaminase	The invention relates to novel heterocyclic compounds and pharmaceutical preparations thereof. The invention further relates to methods of treatment using the novel heterocyclic compounds of the invention.	2033	Method of treating cancer
6/20/2013	US20130157998A1	Heterocyclic inhibitors of glutaminase	The invention relates to novel heterocyclic compounds and pharmaceutical preparations thereof. The invention further relates to methods of treatment using the novel heterocyclic compounds of the invention.	2032	Method of treating neurological and immune diseases
6/12/2014	WO2014089048A1	Treatment of cancer with heterocyclic inhibitors of glutaminase	The invention relates to novel heterocyclic compounds and pharmaceutical preparations thereof and the methods of treating or preventing cancer using the compounds of the invention. Other aspects relate to methods of identifying a cancer patient that may benefit from treatment with a glutaminase inhibitor comprising determining the ratio of glutamate to glutamine, the ratio of glutaminase enzyme to glutamine synthetase or glutaminase activity in cancer cells of the patient.	2033	Method of treating cancer
5/22/2014	WO2014078645A1	Heterocyclic glutaminase inhibitors	Disclosed herein are heterocyclic compounds containing thiadiazole and/or pyridazine rings, as well as pharmaceutical preparations thereof. The compounds herein are further made known to be useful as glutaminase inhibitors with potential uses in treating cancer, immunological and neurological diseases.	2033	Method of treating neurological and immune diseases
5/30/2013	WO2013078123A1	Heterocyclic inhibitors of glutaminase	The invention relates to the heterocyclic compounds of Formula (I) as defined further herein, and pharmaceutical preparations thereof. The invention further relates to methods of treating cancer, immunological or neurological diseases using the heterocyclic compounds of the invention.	2032	Method of treating neurological and immune diseases

Source: USPTO and World Patent Office, and Wells Fargo Securities, LLC

Income Statement

Exhibit 34. Calithera's Income Statement

Calithera Biosciences, Inc. Income Statement
Statement of Operations
(In 000's, except per share data. Fiscal year ends December 31)

Matthew J. Andrews (617) 603-4218

	FY 2013A	H1 2014A	Q3 2014E	Q4 2014E	FY 2014E	FY 2015E	FY 2016E	FY 2017E	FY 2018E	FY 2019E	FY 2020E	FY 2021E	FY 2022E	FY 2023E	FY 2024E	FY 2025E
Revenues																
CB-839 U.S. Sales	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$5,432	$45,178	$101,432	$184,152	$279,765
Royalty on ex-U.S. sales of CB-839	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$2,636	$9,273	$21,729	$39,101
Collaboration revenue on CB-839	$0	$0	$0	$0	$0	$0	$0	$0	$27,750	$3,750	$23,250	$41,250	$21,750	$3,750	$3,750	$3,750
Total revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$27,750**	**$3,750**	**$23,250**	**$46,682**	**$69,564**	**$114,455**	**$209,631**	**$322,616**
Expenses																
Cost of Goods Sold					$0	$0	$0	$0	$0	$0	$0	$543	$4,518	$10,143	$18,415	$27,977
Research and development	$9,900	$7,501	$4,000	$4,500	$16,001	$23,000	$25,000	$30,000	$35,000	$35,000	$37,500	$35,000	$37,500	$40,000	$40,000	$45,000
General and administrative	$2,478	$2,141	$1,050	$1,100	$4,291	$5,200	$6,000	$6,750	$10,000	$20,000	$25,000	$52,500	$62,500	$70,000	$77,500	$82,500
Total Expenses	**$12,378**	**$9,642**	**$5,050**	**$5,600**	**$20,292**	**$28,200**	**$31,000**	**$36,750**	**$45,000**	**$55,000**	**$62,500**	**$88,043**	**$104,518**	**$120,143**	**$135,915**	**$155,477**
Profit/Loss from Operations	**($12,378)**	**($9,642)**	**($5,050)**	**($5,600)**	**($20,292)**	**($28,200)**	**($31,000)**	**($36,750)**	**($17,250)**	**($51,250)**	**($39,250)**	**($41,361)**	**($34,953)**	**($5,688)**	**$73,716**	**$167,140**
Other Income	$1	$2	$2	$5	$9	$73	$50	$867	$1,479	$1,459	$1,117	$1,462	$1,824	$1,728	$1,993	$2,914
Gain on extinguishment of convertible preferred stock	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Net profit (loss) before income tax expense	($12,377)	($9,640)	($5,048)	($5,595)	($20,283)	($28,127)	($30,950)	($35,883)	($15,771)	($49,791)	($38,133)	($39,899)	($33,130)	($3,960)	$75,709	$170,054
Income tax expense	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$18,927	$42,514
Net income/(loss) (GAAP)	**($12,377)**	**($9,640)**	**($5,048)**	**($5,595)**	**($20,283)**	**($28,127)**	**($30,950)**	**($35,883)**	**($15,771)**	**($49,791)**	**($38,133)**	**($39,899)**	**($33,130)**	**($3,960)**	**$56,781**	**$127,541**
EPS (GAAP, diluted)	**($3.03)**	**($1.22)**	**($0.28)**	**($0.31)**	**($1.39)**	**($1.63)**	**($1.71)**	**($1.40)**	**($0.59)**	**($1.85)**	**($1.41)**	**($1.24)**	**($1.03)**	**($0.12)**	**$1.75**	**$3.92**
Shares Outstanding (Basic)	4,083	7,894	17,882	17,907	14,561	17,287	18,107	25,707	25,807	25,907	26,007	31,107	31,207	31,307	31,407	31,507
Shares Outstanding (Diluted)	4,083	7,894	18,903	18,928	15,582	18,309	19,128	26,728	26,828	26,928	27,028	32,128	32,228	32,328	32,428	32,528

Source: Company reports, Form S-1 dated September 25, 2014, and Wells Fargo Securities, LLC estimates

Note: FY 2012A, H1 2013A, FY 2013A, H1 2014A are all based on information included in the Calithera, Biosciences, Inc. S-1 dated September 25, 2014. All revenues are probability-weighted.

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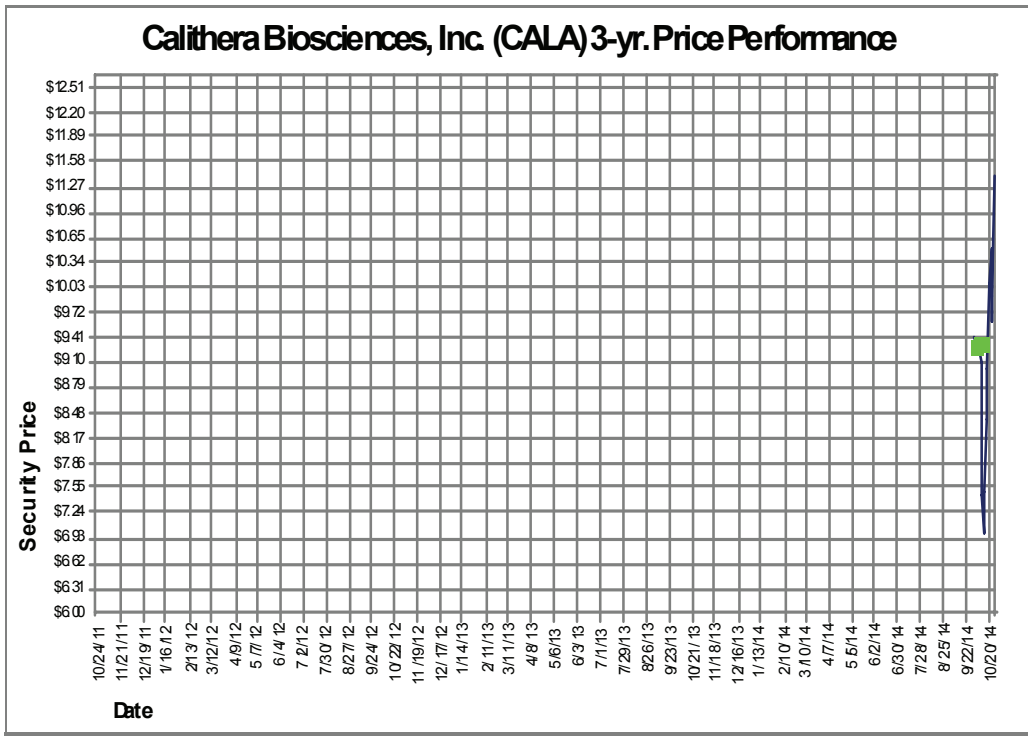
Required Disclosures



	Date	Publication Price ($)	Rating Code	Val. Rng. Low	Val. Rng. High	Close Price ($)
❐	10/3/2014		IPO at $10.00			

Source: Wells Fargo Securities, LLC estimates and Reuters data

Symbol Key

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

Rating Code Key

1	Outperform/Buy	SR	Suspended
2	Market Perform/Hold	NR	Not Rated
3	Underperform/Sell	NE	No Estimate

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

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2=Market Perform: The stock appears appropriately valued, and we believe the stock's total return will be in line with the market over the next 12 months. HOLD
3=Underperform: The stock appears overvalued, and we believe the stock's total return will be below the market over the next 12 months. SELL

SECTOR RATING

O=Overweight: Industry expected to outperform the relevant broad market benchmark over the next 12 months.
M=Market Weight: Industry expected to perform in-line with the relevant broad market benchmark over the next 12 months.
U=Underweight: Industry expected to underperform the relevant broad market benchmark over the next 12 months.

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As of: October 24, 2014

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