Calithera Presents Preclinical Study Findings for CB-839 at the 56th American Society of Hematology Annual Meeting

December 8, 2014

-Potential Biomarkers of Response to CB-839 Identified in Myeloma Cells

-Synergy of CB-839 With Pomalidomide Demonstrated in Multiple Myeloma Models


"Data presented at this week's ASH provides us with valuable insights into cellular metabolic properties that could ultimately direct our development of CB-839 towards the patients most likely to benefit from treatment. We have identified pyruvate carboxylase expression and functional read-outs of the mTORC1 pathway as possible biomarkers in our clinical studies of CB-839. Additionally, based on the pronounced synergy we observed preclinically with CB-839 and IMiDs, we are planning to initiate a Phase 1b trial treating myeloma patients with CB-839 plus pomalidomide and dexamethasone," said Susan Molineaux, PhD, President and Chief Executive Officer of Calithera.

Preclinical data was presented in a poster titled, "Biomarkers of Response to the Glutaminase Inhibitor CB-839 in Multiple Myeloma Cells," on December 7, 2014 (Abstract #3429). High pyruvate carboxylase expression conferred inherent resistance to CB-839; those myeloma cells that did not express high levels of pyruvate carboxylase were sensitive to CB-839. In addition, the baseline metabolic profiles of CB-839 sensitive multiple myeloma cells were different from that of insensitive cells, suggesting that nutrient state and energy storage level in myeloma cells is an important factor in determining response to CB-839. Finally, the metabolic stress induced by CB-839 led to sustained inhibition of the nutrient sensor mTORC1 in sensitive cells, with downstream effects on protein synthesis, nucleotide production and glycolysis.

Calithera also presented today at ASH the results of a study investigating the preclinical anti-tumor activity of CB-839 in combination with pomalidomide, demonstrating synergistic antiproliferative effects in IMiD-resistant cells in a poster titled, "Glutaminase Inhibitor CB-839 Synergizes with Pomalidomide in Preclinical Multiple Myeloma Models." (Abstract #4720). The combination of CB-839 and pomalidomide produced enhanced effects on metabolic and signal transduction pathways likely contributing to the synergistic anti-proliferative activity. In addition, in a multiple myeloma xenograft model, CB-839 showed significant single agent anti-tumor efficacy and displayed enhanced anti-tumor activity when combined with pomalidomide.

In addition, two posters were presented by Calithera's collaborators. Details for the presentations are as follows:

**Anti-Myeloma Activity of a Novel Glutaminase Inhibitor CB-839**

Abstract #3439

Deepika Sharma Das, Ph.D., Dana Farber Cancer Institute

Poster Session 652 Myeloma: Pathophysiology and Pre-Clinical studies, excluding Therapy: Poster II

**Efficacy of Novel Glutaminase Inhibitor CB-839 in Acute Myeloid Leukemia**

Abstract #3763

Polina Matre, Ph.D., MD Anderson Cancer Center

Poster Session 616 Acute Myeloid Leukemia: Novel Therapy, excluding Transplantation: Poster III

About Calithera Biosciences

Calithera Biosciences is a clinical-stage company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology. Calithera's lead clinical candidate, CB-839, is a first-in-class inhibitor of glutaminase, a critical enzyme in tumor metabolism, and is currently being tested in patients with solid and hematological cancers. Calithera Biosciences is headquartered in South San Francisco. For more information about Calithera Biosciences, please visit [www.calithera.com](http://www.calithera.com).

Forward Looking Statements

This news release contains forward-looking statements by Calithera that involve risks and uncertainties. These statements include those related to the advancement of Calithera's tumor metabolism and tumor immunology therapeutics through clinical development and Calithera's plan to initiate a Phase 1b trial treating myeloma patients with CB-839 plus pomalidomide and dexamethasone; Actual results may differ from Calithera's expectations and important factors that could cause actual results to differ materially. Calithera's product candidates may not progress through clinical development or receive required regulatory approvals within expected timelines or at all. In addition, clinical trials may not confirm any safety, potency or other product characteristics described or assumed in this press release. In particular, future clinical trials may not show the synergy Calithera observed preclinically with CB-839 and IMiDs. Furthermore, Calithera's product candidates may not be beneficial to patients or successfully commercialized. The failure to meet expectations with respect to any of the foregoing matters may have a negative effect on Calithera's stock price. Additional information concerning these and other risk factors affecting Calithera's business can be found in Calithera's Quarterly Report on Form 10-Q for the period ended September 30, 2014 and other periodic filings with the Securities and Exchange Commission at [www.sec.gov](http://www.sec.gov). These forward-looking statements are not guarantees of future performance and speak only as of the date hereof, and, except as required by law, Calithera disclaims any obligation to update these forward-looking statements to reflect future events or circumstances.

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