



## Calithera Biosciences Announces Four Abstracts Selected for Presentation at the Society for Immunotherapy of Cancer (SITC) 2016 Annual Meeting

November 11, 2016

### CB-1158 Pharmacodynamic Effects Observed in Patients

SOUTH SAN FRANCISCO, Calif., Nov. 11, 2016 (GLOBE NEWSWIRE) -- Calithera Biosciences, Inc. (Nasdaq:CALA), a clinical stage biotechnology company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer, today announced that data for its drug candidates CB-839, the company's novel glutaminase inhibitor, and CB-1158, the company's novel arginase inhibitor, will be presented at the Society for Immunotherapy of Cancer (SITC) 2016 Annual Meeting, which is being held from November 9-13, 2016 in National Harbor, Maryland.

"Both CB-839 and CB-1158 have the distinction of targeting metabolic and immune checkpoints which we believe, through rational combinations, have the potential to be transformational in the treatment of cancer. CB-839 and CB-1158 are each in clinical trials with cohorts planned in combination with approved immunotherapy agents," said Susan Molineaux, Ph.D., President and Chief Executive Officer of Calithera. "We are pleased that CB-1158 shows significant pharmacodynamic effects in patients at the first dose level tested."

Preclinical CB-839 data will be presented in a poster titled, "Targeting tumor glutamine metabolism with CB-839 enhances the efficacy of immune checkpoint inhibitors," by Andy MacKinnon, Ph.D., Calithera Biosciences (Poster #230). Included in the presentation are data that provide further insights into the mechanism by which inhibition of glutaminase by CB-839 enhances T-cell activation and increases the anti-tumor activity of anti-PD-L1 and anti-PD-1 antibodies. Glutamine deprivation during T-cell activation was shown to block Myc expression and Myc-driven metabolic re-programming, and to promote expression of T-cell suppressive markers such as BTLA, CTLA-4, PD-1, and CD73. In two syngeneic animal models, CT26 (colon cancer) and B16 (melanoma) the combination of CB-839 and anti-PD-L1 or anti-PD-1 showed significantly enhanced anti-tumor activity over checkpoint inhibition alone resulting in increased tumor regressions in the CT26 model. Depletion of CD8+ T-cells from these tumor-bearing animals reversed the anti-tumor effects of the combination, confirming an immune-mediated mechanism of action.

CB-1158 data will be presented in a poster titled, "Arginase inhibitor CB-1158 alleviates immunosuppression and enhances anti-tumor responses as a single agent and in combination with other immunotherapies," by Amani Makkouk, Ph.D., Calithera Biosciences (Poster #231). Arginase is expressed in myeloid derived suppressor cells (MDSCs) and exerts an immunosuppressive effect on T-cells and NK cells by depleting arginine and blocking activation. Tumor cell infiltrates in patients with solid tumor cancers contain significant numbers of arginase-expressing MDSCs; as a result, these patients have increased levels of plasma arginase and decreased levels of plasma arginine compared to healthy individuals. CB-1158, a highly selective, orally bioavailable, small molecule inhibitor of human arginase with nanomolar potency, has single agent immune-mediated efficacy in multiple syngeneic animal models. Inhibition of tumor growth was accompanied by an increase in the local concentration of arginine, and the induction of multiple pro-inflammatory changes in the tumor microenvironment. Treatment with CB-1158 also enhanced the anti-tumor activity of adoptive T-cell therapy, checkpoint blockade and chemotherapy in these animal models. CB-1158 is currently being tested in a Phase 1 clinical trial in patients with solid tumors. Three patients in the first cohort were treated with 50 mg of CB-1158 twice daily. This dose was well-tolerated and was pharmacologically active, resulting in sustained elevation of arginine in the plasma of all three patients. The trial is continuing to enroll patients to complete the dose escalation phase of the study, to be followed by combination studies with a PD-1 antibody.

In addition, two posters describing trial design will be presented during the "Clinical Trials in Progress" session:

#### **CX-1158-101: A first-in-human phase I study of a small molecule inhibitor of arginase (CB-1158) as monotherapy and in combination with an anti-PD-1 checkpoint inhibitor in patients with solid tumors**

Presenter: Siqing Fu, M.D., Ph.D., University of Texas, MD Anderson Cancer Center, Poster #155

#### **CX-839-004: A phase I/II study of the safety, pharmacokinetics, and pharmacodynamics of the glutaminase inhibitor CB-839 combined with nivolumab in patients with renal cell carcinoma, melanoma, and non-small cell lung cancer**

Presenter: Elaine Lam, M.D., University of Colorado, Denver, Poster #166

#### About Calithera Biosciences

Calithera Biosciences, Inc. is a clinical-stage pharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer. Calithera's lead product candidate, CB-839, is a potent, selective, reversible and orally bioavailable inhibitor of glutaminase. CB-839 takes advantage of the pronounced dependency many cancers have on the nutrient glutamine for growth and survival. It is currently being evaluated in Phase 1/2 clinical trials in combination with standard of care agents. CB-1158 is a first-in-class immuno-oncology metabolic checkpoint inhibitor targeting arginase, a critical immunosuppressive enzyme responsible for T-cell suppression by myeloid-derived suppressor cells. Arginase depletes arginine, a nutrient that is critical for the activation, growth and survival of the body's cancer-fighting immune cells, known as cytotoxic T-cells. CB-1158 is currently in a Phase I clinical trial. Calithera is headquartered in South San Francisco, California. For more information about Calithera, please visit [www.calithera.com](http://www.calithera.com).

#### Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "anticipate," "estimate," "intend," "poised" and similar expressions (as well as other words or expressions referencing future events, conditions, or circumstances) are intended to identify forward-looking statements. Examples of these statements include the ability for CB-839 and CB-1158 to be transformational in the treatment of cancer, the pharmacodynamics effects of CB-1158, the potential for increases in the number of tumor regressions or inhibition of tumor growth and the efficacy of CB-839 and CB-1158. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. The potential product candidates that Calithera develops 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. Such 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 most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, 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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