Calithera Biosciences Presents Preclinical Data for CB-839Activity and Glutaminase Inhibition in Solid and Hematologic Tumors

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South San Francisco, CA; March 18, 2014 â€“ Calithera Biosciences, a clinical-stage biotechnology company focused on the development of novel cancer therapeutics, today announced the presentation of preclinical data for its lead anti-cancer therapeutic candidate, CB-839, at the Keystone Symposium on Tumor Metabolism being held in Whistler, Canada from March 16-21, 2014. CB-839 is a potent, selective, orally bioavailable glutaminase inhibitor that interferes with tumor metabolism and blocks cancer cell growth and survival.

â€œThe more we learn about the role of glutaminase in tumor metabolism, the more promising glutaminase inhibition appears to be as a target for novel anti-cancer therapeutics,â€said Susan Molineaux, PhD, President and Chief Executive Officer of Calithera Biosciences. â€œData being presented at this weekâ€™s Keystone Symposium demonstrate the clear dependence of certain tumor cell types on glutaminase for growth and survival, and provide us with valuable insights into the differences in tumor cell metabolism that may dictate sensitivity to glutaminase inhibition. Ultimately, these data will inform our clinical development programs and guidepotential predictive biomarker efforts.â€

Preclinical data detailing CB-839 activity in solid and hematologic tumor types were presented in a poster titled â€œAntiproliferative Activity of the Glutaminase Inhibitor CB-839 In Glutamine-Dependent Solid and Hematological Tumor Cell Linesâ€on March 17, 2014. Triple-negative breast cancer (TNBC) cell lines were markedly more sensitive to CB-839 than ER-positive cell lines, and sensitivity was directly correlated to the level of glutaminase expression and the baseline ratio of glutamate to glutamine prior to drug treatment. Primary tumors from TNBC patients had higher glutaminase expression and higher glutamate to glutamine ratios than tumors from other breast cancers, suggesting that human TNBC tumors are more dependent on glutamine metabolism relative to ER-positive tumors. Expression analysis across a wide array of human primary tumors showed that a similar glutamine utilization profile exists in many other tumor types, including non-small cell lung cancer, mesothelioma, multiple myeloma and other Bcell malignancies

Calithera will also present data on the utility of xenograft models in predicting glutaminase dependent metabolism and CB-839 sensitivity. In two myeloma cell lines, both sensitive to CB-839 *in vitro*, one cell line remained metabolically stable and sensitive to drug when implanted in mice, while the other cell line responded to implantation by altering its metabolic pattern significantly. In the latter cell line, higher levels of metabolites associated with glycogen breakdown and fatty acid oxidation appeared to render the tumor insensitive to growth inhibition with CB-839. The metabolite profile of the sensitive model may reflect a nutrient utilization pattern indicative of glutaminase dependence that could be exploited to identify CB-839-sensitive tumors. Furthermore, the identification of metabolic pathways adopted by the insensitive model offers the potential to develop combination strategies that could restore a tumorâ€™s dependence on glutamine. These data will be presented on March 18 in a poster titled â€œMetabolomic Profiling of Xenograft Tumors following Treatment with the Glutaminase Inhibitor CB-839â€.

Earlierthis year, Calithera commenced patient dosing in its Phase 1clinical program designed to determine safety and tolerability of CB-839and to establish a dose for Phase 2 studies. Calithera is conducting three Phase 1 studies in parallel: in patients with advanced solid tumors, with advanced multiple myeloma and non-Hodgkinâ€™s lymphoma, and with acute leukemias. All three Phase 1 clinical trials are single-arm, open-label dose escalation studies that allow for expansion in specific tumor types once the recommended Phase 2dose is reached.

About Calithera Biosciences
Calithera Biosciences, Inc. is a clinical-stage company focused on the discovery, development and commercialization of first-in-class small molecule oncology therapeutics. The company is building a pipeline of targeted anti-cancer compounds that inhibit pathways critical to tumor growth and survival. Caliteraâ€™s lead clinical candidate, CB-839, blocks glutaminase, an enzyme critical to tumor metabolism, and is currently being tested in patients with advanced solid and hematological cancers. Calithera Biosciences is headquartered in South San Francisco. For more information about

Calithera Biosciences, please visit www.calithera.com

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