



New Data Presented at ESMO Congress 2019 from the Arginase Inhibitor INCB001158 Alone and in Combination with Pembrolizumab

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Responses observed in patients with microsatellite stable (MSS) colorectal cancer, a disease not historically sensitive to checkpoint inhibition

SOUTH SAN FRANCISCO, Calif., Sept. 29, 2019 (GLOBE NEWSWIRE) -- Calithera Biosciences, Inc. (Nasdaq: CALA), a clinical stage biotechnology company focused on discovering and developing novel small molecule drugs for the treatment of cancer and other life-threatening diseases, today announced the presentation of new data from the investigational first-in-class oral arginase inhibitor INCB001158 as a monotherapy and in combination with the checkpoint inhibitor pembrolizumab in microsatellite stable (MSS) colorectal carcinoma patients. The data were presented during an oral Proffered Paper session at the European Society for Medical Oncology (ESMO) Congress 2019 taking place in Barcelona, Spain (Abstract #4400). Calithera has a global collaboration and license agreement with Incyte Corporation for the joint research, development and commercialization of INCB001158 in hematology and oncology.

"We are pleased to share initial data from the trial of INCB001158 in MSS colorectal carcinoma that is refractory to standard therapies, a disease that has very low historical average response rates to checkpoint inhibitors such as pembrolizumab," said Susan Molineaux, PhD, president and chief executive officer of Calithera. "We are pleased with the progress of this program as we seek to develop a first-in-class product for patients with multiple types of solid tumors."

Calithera and Incyte are collaborating to conduct this Phase 1 study evaluating INCB001158 as monotherapy and in combination with the PD-1 inhibitor pembrolizumab in checkpoint inhibitor refractory and naïve advanced/metastatic solid tumors. Data were presented as of the data cut-off of July 22, 2019. The study was designed as a dose escalation of INCB001158 alone and in combination with pembrolizumab followed by expansion cohorts which followed a Simon 2 Stage design. There were three monotherapy expansion cohorts (non-small cell lung cancer, colorectal carcinoma and other solid tumors) and eight combination expansion cohorts, including PD-(L)1-naïve (MSS colorectal carcinoma, head and neck cancer, gastric cancer, mesothelioma) and PD-(L)1 refractory (non-small cell lung cancer, urothelial carcinoma, melanoma, and MSI colorectal carcinoma) patients.

Combination Results

- The PD-(L)1-naïve MSS colorectal carcinoma (CRC) patient cohort has advanced to stage 2 of a Simon 2-stage design. Among 43 response-evaluable patients who had received a median of 3 prior therapies, 3 patients achieved a confirmed partial response (7%); the historical overall response rate is 0-1% in second- and third-line MSS CRC patients treated with checkpoint inhibitor therapies. Two of the three responders are ongoing at the time of data cutoff with a duration of response of 2.4+ and 7+ months respectively. The third responder had a duration of response of 6.7 months. The six month PFS rate for the cohort was 20%.
- Pharmacodynamic increases in total intratumoral CD8⁺ cells were seen post-treatment with INCB001158 + pembrolizumab in MSS CRC patients.

Monotherapy Results

- The colorectal carcinoma monotherapy cohort has advanced to stage 2 of a Simon 2-stage design. Among 33 response-evaluable MSS CRC patients, one patient achieved a confirmed partial response (3%) and one patient achieved stable disease lasting seven months. Both patients had disease progression within six months on their immediately preceding line of therapy. The disease control rate for the monotherapy MSS CRC cohort was 27%.
- INCB001158 inhibited plasma arginase activity at all doses and induced dose-related increases in plasma arginine, including a mean three-fold increase at the recommended phase 2 dose of 100 mg bid.

Safety

- A total of 85 patients with advanced solid tumors were treated with INCB001158 as a monotherapy in doses of 50 to 150mg bid and were evaluable for safety. A maximum tolerated dose was not reached. Immune-related adverse events included one dose-limiting toxicity (DLT) each of Grade 2 malaise (at 150mg) and Grade 3 colitis (100mg). Clinically significant urea cycle inhibition was not seen.

- A total of 114 PD-(L)1-naïve and PD-(L)1 refractory patients were treated in INCB001158 in combination with pembrolizumab and evaluable for safety across multiple disease specific cohorts. The overall frequency and severity of immune related adverse events was consistent with the pembrolizumab safety profile.

About INCB001158 (CB-1158)

INCB001158 (CB-1158) is an investigational first-in-class, novel small molecule arginase inhibitor. Arginase is an enzyme that suppresses the immune-mediated destruction of tumors by depleting levels of a key amino acid, L-arginine, from the tumor microenvironment. A number of cell types in the tumor microenvironment, including myeloid-derived suppressor cells, macrophages, and neutrophils, can secrete arginase. L-arginine deprivation can act via nutrient sensor pathways to exert several suppressive effects on T-cell function, inhibiting proliferation, decreasing cytokine production, and diminishing expression of the T-cell receptor CD3 ζ chain. Arginase activity may thus impair T-cell mediated anti-tumor responses. INCB001158 is being developed in a global collaboration with Incyte Corporation.

About Calithera

Calithera Biosciences is a clinical-stage biopharmaceutical company pioneering the discovery and development of targeted therapies that disrupt cellular metabolic pathways to preferentially block tumor cells and enhance immune-cell activity. Driven by a commitment to rigorous science and a passion for improving the lives of people impacted by cancer and other life-threatening diseases, Calithera is advancing a pipeline of first-in-clinic, oral therapeutics to meaningfully expand treatment options available to patients. Calithera is headquartered in South San Francisco, California. For more information about Calithera, please visit 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. These statements include those related to the safety, tolerability and efficacy of Calithera's product candidates, the overall advancement of Calithera's product candidates in clinical trials, the unmet need in the treatment of patients with advanced disease, and Calithera's plans, and those of its collaboration partners, to continue development of its product candidates. 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 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. 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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