



## Data From Randomized Phase 2 ENTRATA Study Demonstrate Telaglenastat with Everolimus Improves Progression-Free Survival in Renal Cell Carcinoma

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- *Data shared today in oral presentation at ESMO Congress 2019 show telaglenastat doubles median progression-free survival (PFS) in heavily pre-treated patients with advanced disease, reduced risk of death by 36% (HR=0.64, p=0.079 one-sided)*
- *First glutaminase inhibitor to demonstrate clinical activity for treatment of cancer*

SOUTH SAN FRANCISCO, Calif., Sept. 28, 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, presented today supporting data for its previously reported positive results from its randomized placebo-controlled Phase 2 ENTRATA study of telaglenastat (CB-839) in combination with everolimus in patients with advanced renal cell carcinoma (RCC). The telaglenastat-everolimus combination doubled the median progression-free survival (PFS) in heavily pre-treated patients with advanced RCC and had a well-tolerated safety profile. Telaglenastat is the first glutaminase inhibitor to demonstrate clinical activity for the treatment of cancer.

Calithera announced top-line results from the ENTRATA trial in June. Data from the study were accepted as a late-breaker abstract and will be shared for the first time this morning during an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2019 in Barcelona, Spain (#LBA54).

"Outcomes for late-line metastatic renal cell carcinoma are often poor using currently available medications with similar mechanism of action," said Chung-Han Lee, MD, PhD, Memorial Sloan Kettering Cancer Center, who will present the data. "New treatments with novel mechanisms of action are greatly needed for this patient population. The results from the randomized ENTRATA trial demonstrate activity of telaglenastat in RCC and provide proof of concept for glutaminase inhibition as a new mechanism of action that may improve outcomes for patients with this disease."

"We continue to be encouraged by these data, which suggest that glutaminase inhibition – and telaglenastat in particular - could offer advanced RCC patients a novel therapeutic option," said Susan Molineaux, PhD, president and chief executive officer of Calithera. "ENTRATA demonstrates a clinically meaningful improvement in progression-free survival among patients with advanced disease who have been treated with many prior lines of therapy. We are evaluating telaglenastat in the ongoing CANTATA trial in combination with cabozantinib for patients with advanced clear cell RCC, and we look forward to learning how telaglenastat performs in this setting."

Key demographics in patients enrolled in the phase 2 ENTRATA study were balanced between the two treatment arms (telaglenastat in combination with everolimus versus placebo with everolimus) and were heavily pre-treated, with a median of three prior lines of therapy for advanced metastatic disease including 70% (72% vs. 65%) with two or more prior tyrosine kinase inhibitors (TKI), and 68% (70% vs. 65%) with intermediate/poor MSKCC prognostic score. Eighty-eight percent of patients received prior PD-1/PD-L1 therapy (91% vs. 83%).

When added to everolimus, telaglenastat doubled the median PFS to 3.8 months as compared to 1.9 months for everolimus alone and reduced the risk of disease progression or death by 36% (HR=0.64, p=0.079 one-sided). The primary endpoint of the trial was PFS per investigator assessment with a predetermined threshold of p≤0.2 one-sided. Overall response per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v.1.1) was 2.2% vs. 0%, and stable disease was 56.5% vs. 47.8%. The secondary endpoint of overall survival is not yet mature.

Frequency of all-grade adverse events in the telaglenastat-containing arm were comparable to that of everolimus alone. Grade 3 or higher adverse events occurred in 80.4% of patients in the telaglenastat plus everolimus arm versus 60.9% in the everolimus plus placebo arm. The most frequently reported Grade ≥3 adverse events in the treatment versus control arms, respectively, were anemia (17.4% vs. 17.4%), pneumonia (6.5% vs. 4.3%), abdominal pain (6.5% vs. 0%), thrombocytopenia (6.5% vs. 0%), and fatigue (4.3% vs. 8.7%). Adverse events leading to discontinuation of any study drug were comparable (28.3% vs. 30.4%).

The ENTRATA trial ([NCT03163667](#)) is a randomized, double-blind Phase 2 trial designed to evaluate the efficacy and safety of telaglenastat in combination with everolimus versus placebo with everolimus in patients with advanced clear cell RCC who have been treated with at least two prior lines of systemic therapy, including at least one VEGFR-targeted TKI. Patients were randomized in a 2:1 ratio, and stratified by prior TKI treatment and MSKCC prognostic score. The trial enrolled 69 patients at multiple centers in the United States.

Telaglenastat is an investigational first-in-class glutaminase inhibitor specifically designed to block glutamine consumption in tumor cells. RCC tumors commonly exhibit metabolic alterations that increase their dependence on glutamine. In preclinical studies, telaglenastat produced synergistic antitumor effects when used in combination with standard-of-care RCC therapies.

Telaglenastat is also being investigated in the CANTATA trial (NCT03428217), a global, randomized, double-blind trial designed to evaluate the efficacy and safety of telaglenastat in combination with cabozantinib versus placebo with cabozantinib in patients with advanced or metastatic RCC who have been treated with one or two prior lines of systemic therapy including at least one vascular endothelial growth factor tyrosine kinase inhibitor or the combination of nivolumab and ipilimumab. In April 2018, the U.S. Food and Drug Administration granted Fast Track designation to telaglenastat

in this indication. The primary endpoint is progression-free survival by blinded independent review, and a key secondary endpoint is overall survival. Calithera plans to report top-line efficacy and safety data from the trial in the second half of 2020.

A link to a copy of the presentation is available on Calithera's corporate website at <https://www.calithera.com/publications-and-presentations>.

#### Conference Call Information

Calithera will host an update conference call Monday, September 30, at 8:30 a.m. Eastern Time / 5:30 a.m. Pacific Time. The call may be accessed by dialing (855) 783-2599 (domestic) or (631) 485-4877 and referring to conference ID 1469186. To access the live audio webcast or the subsequent archived recording, visit the Investors section of the Calithera website at [www.calithera.com](http://www.calithera.com). The webcast will be recorded and available for replay on Calithera's website for 30 days.

#### 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 cell growth 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](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. These statements include those related to the potential for telaglenastat to be developed in combination with therapeutics, such as everolimus or cabozantinib, to improve patient outcomes, safety, tolerability and efficacy of telaglenastat; the overall advancement and timing of telaglenastat in clinical trials; and the unmet need in the treatment of patients with advanced RCC. 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](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.

SOURCE: Calithera Biosciences, Inc.

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