Calithera Presents Interim Data from Phase 1b Trial of Arginase Inhibitor CB-280 in Cystic Fibrosis at NACFC 2021

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-- CB-280 was well-tolerated, showed linear PK and demonstrated robust dose-related PD effects
-- Encouraging trends seen in disease biomarkers including increased FeNO and decreased sweat chloride
-- Early positive trend seen in FEV1, a safety endpoint

SOUTH SAN FRANCISCO, Calif., Nov. 01, 2021 (GLOBE NEWSWIRE) -- Calithera Biosciences, Inc. (Nasdaq: CALA), a clinical-stage biopharmaceutical company, today shared interim safety and efficacy results from a Phase 1b, randomized, double-blind, placebo-controlled, dose-escalation trial evaluating CB-280, the company's investigational arginase inhibitor, in adults with cystic fibrosis (CF). The data were shared in a poster presentation at the North American Cystic Fibrosis Foundation Conference (NACFC; Abstract 529).

"There remains a high unmet need for novel anti-infective treatment approaches for people with cystic fibrosis," said Susan Molineaux, Ph.D., president and chief executive officer of Calithera. "It's incredibly rewarding to share these first clinical data from our CB-280 program, which further validate the compound's novel mechanism of action, as well as its potential to become a new therapeutic option for all people with CF, regardless of the disease genotype."

CF is a genetic disease that causes persistent lung infections, resulting in progressive impairment of lung function over time. Research in CF patients has demonstrated that increased arginase activity correlates directly with worsened lung function and decreased airway nitric oxide (NO), promoting pathogen colonization. CB-280, a selective, orally dosed arginase inhibitor, is a novel, first-in-class approach to enhance airway NO levels to combat chronic airway infections and improve lung function in people with CF.

At NACFC, data were presented on the first 24 subjects (18 treated with CB-280, six with placebo) participating in the ongoing, Phase 1b dose-escalation trial in adults with CF. Key eligibility criteria for patients included chronic lung infection and current treatment with a stable CF medication regimen including cystic fibrosis transmembrane conductance regulator (CFTR) modulators. Each dose cohort consisted of eight subjects randomized 3:1 to CB-280 or placebo dosed twice daily for 14 days. At the completion of each dose cohort, unblinded data were reviewed by an Independent Data Safety Monitoring Committee (IDMC) convened by the Cystic Fibrosis Foundation (CFF).

Data were presented for 50mg BID, 100mg BID and 200mg BID dose levels. The study enrolled subjects with a broad spectrum of CFTR genotypes, including nonsense mutations. Notably, 91% of subjects were already on CFTR modulator therapy with Trikafta® (elexacaftor/tezacaftor/ivacaftor) or Kalydeco®(ivacaftor). CB-280 had a well-tolerated safety profile across all three dose levels, and all 18 subjects receiving CB-280 completed treatment without treatment interruptions or premature discontinuations. Changes in forced expiratory volume in one second (FEV1) were assessed as a safety endpoint. A pooled analysis of treatment vs. placebo showed a positive trend in FEV1 compared to placebo.

CB-280 demonstrated linear pharmacokinetics with plasma exposure increasing proportionally with dose. Complete and continuous target inhibition in plasma was achieved at the 100 mg dose and above. CB-280 also demonstrated robust pharmacodynamic effects, with rapid and significant dose-proportional increases in plasma arginine, the key driver of NO production.

Biomarkers of arginase inhibition showed trends that further substantiate the proposed mechanism of action. There was a trend toward increased FeNO and decreased sweat chloride in CB-280 treated subjects. Changes in sweat chloride were measured as an exploratory endpoint, based on published data showing enhanced CFTR function with arginase inhibition in human bronchial epithelial cells.

"I am encouraged by these initial data of CB-280 in subjects with CF and chronic infection, particularly its well-tolerated safety profile and positive early trends in important disease markers including FeNO, FEV1, and sweat chloride," said Scott Donaldson, M.D., Hubert E. Hatcher Distinguished Professor of Medicine, Division of Pulmonary Diseases and Critical Care Medicine, University of North Carolina, Chapel Hill, NC and a study investigator. "Although early, seeing such trends with a short dosing duration in subjects already on CFTR modulators, and across different CF disease genotypes is noteworthy. I look forward to expanding our understanding of this investigational, novel arginase inhibitor through this ongoing trial."

The study is ongoing with Cohort 4 (300mg BID) on track to complete enrollment by the end of 2021.

A recorded presentation of the poster, "A phase 1b, randomized, double-blind, placebo-controlled, dose escalation trial of CB-280, an arginase inhibitor, in patients with cystic fibrosis," will be available to NACFC registered attendees. Study authors will be available via live video chat on Wednesday, November 3, 2021, from 1:10-1:50 p.m. ET. Additionally, a copy of the poster will be available at https://www.calithera.com/publications-and-presentations/ in the publications section.

About Calithera
Calithera Biosciences is a clinical-stage, precision oncology biopharmaceutical company developing targeted therapies to redefine treatment for biomarker-specific patient populations. 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 robust pipeline of investigational, small molecule oncology compounds with a biomarker-driven approach that targets genetic vulnerabilities in cancer cells to deliver new therapies for patients suffering from aggressive hematologic and solid tumor cancers for which there are currently limited treatment options.

Calithera is headquartered in South San Francisco, California. For more information about Calithera, please visit www.calithera.com.

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