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Cascadian Therapeutics Amends HER2CLIMB Phase 2 Trial of Tucatinib in Metastatic HER2-Positive Breast Cancer to Support Registration

Updated Data from Phase 1b Triplet Combination Trial at SABCS; Increased Median PFS to 7.8 Months and ORR to 61 Percent; Median Duration of Response (MDR) at 10 Months in Third-line Setting for Patients With and Without Brain Metastases

HER2CLIMB Amended to Single Pivotal Randomized Trial to Assess Progression-Free Survival (PFS) as Primary Endpoint

SAN ANTONIO, Texas, Dec. 07, 2016 (GLOBE NEWSWIRE) -- Cascadian Therapeutics, Inc. (NASDAQ:CASC), a clinical-stage biopharmaceutical company, today announced that following a recent meeting with the U.S. Food and Drug Administration (FDA) and discussions with the Company's external Steering Committee, it has amended the HER2CLIMB Phase 2 clinical trial of tucatinib (also known as ONT-380) by increasing the sample size so that, if successful, the trial could serve as a single pivotal study to support registration. This decision is supported by the most recent data from the Company's ongoing Phase 1b study evaluating the same "triplet combination" therapy being investigated in the amended Phase 2 trial, which is tucatinib in combination with capecitabine and trastuzumab for patients with metastatic or locally advanced HER2-positive breast cancer, including patients with and without brain metastases. Tucatinib is an oral, small molecule kinase inhibitor that is highly selective for HER2 without significant inhibition of EGFR.

HER2CLIMB is an ongoing randomized, controlled pivotal trial evaluating tucatinib in combination with trastuzumab (Herceptin®) and capecitabine (Xeloda®) in heavily pre-treated patients with advanced HER2-positive breast cancer with or without brain metastases.

"We are extremely pleased with the outcome of our recent interactions with the FDA, and we have decided to amend the current Phase 2 clinical trial of tucatinib so that, if successful, HER2CLIMB could serve as a single pivotal registration trial and potentially provide us with a more efficient path to market," commented Scott Myers, President and CEO of Cascadian Therapeutics. "We look forward to continuing a collaborative relationship with the agency and our clinical investigators as we advance the development of tucatinib in combination in the third-line metastatic breast cancer setting where there is no single standard-of-care and a need for more tolerable therapeutic options. The improvement in the updated data from our Phase 1b "triplet combination" study reinforces our strategy with tucatinib in this patient population."

Updated Phase 1b trial results for the triplet combination show that the combination (tucatinib with capecitabine and trastuzumab) continues to be well tolerated, with the updated median progression-free survival (PFS) increasing to 7.8 months, an overall response rate (ORR) of 61 percent and a median duration of response (MDR) of 10 months. Patients in the Phase 1b triplet combination previously received a median of 3 HER2-targeted agents, such as trastuzumab, pertuzumab, lapatinib or T-DM1. Poster presentations on the amended HER2CLIMB pivotal trial and the updated Phase 1b "triplet combination" trial data will be presented at the 2016 San Antonio Breast Cancer Symposium (SABCS), December 6-10, 2016.

"The more mature dataset from the Phase 1b trial continues to show tucatinib may be combined with other current targeted therapies to achieve durable responses in patients who have received multiple prior lines of therapy," said Erika Hamilton, M.D., Director of Breast and Gynecology Cancer Research at Sarah Cannon Research Institute. "Tucatinib in combination appears to be well-tolerated, potentially making it a highly desirable HER2 therapy for a patient population that vitally needs new options. An active agent showing systemic activity, with a tolerable safety profile and early signs of activity in HER2-positive brain metastases, would represent a meaningful advancement in treating metastatic breast cancer."

HER2CLIMB Pivotal Trial

HER2CLIMB is a randomized (2:1), double-blind, controlled pivotal clinical trial comparing tucatinib vs. placebo in combination with capecitabine and trastuzumab in patients with locally advanced or metastatic HER2-positive breast cancer who have had prior treatment with a taxane, trastuzumab, pertuzumab and T-DM1. Following a meeting with the FDA, the primary endpoint remains PFS based upon independent radiologic review, and the sample size will increase to approximately 480 patients, including patients already enrolled in the trial. Key objectives related to assessing activity in

brain metastases include a key secondary endpoint of PFS in a subset of patients with brain metastases. All patients will be followed for overall survival. HER2CLIMB is currently enrolling in the United States and Canada and is expected to expand into Europe, Australia and Israel. Details of the amended HER2CLIMB clinical trial design will be presented in a poster session (OT1-02-09) at SABCS on Wednesday, December 7, 2016 beginning at 5:00 p.m. CST.

Updated Phase 1b Triplet Study Findings at SABCS

Results reported in June 2016 showed a median PFS of 6.3 months and ORR of 58 percent. Updated data from the SABCS poster (P4-21-01) of the Phase 1b study show encouraging safety and anti-tumor activity in patients with and without brain metastases, with an updated median PFS of 7.8 months (a 24 percent improvement over prior median PFS), ORR of 61 percent and a median duration of response of 10 months. Patients with and without brain metastases had similar response rate. The combination of tucatinib with trastuzumab and capecitabine was well-tolerated. Most treatment-emergent adverse events were Grade 1, with few tucatinib dose reductions and no required prophylactic use of anti-diarrheal agents. Updated results will be presented in a poster session at SABCS on Friday, December 9, 2016 beginning at 7:30 a.m. CST.

About Tucatinib

Tucatinib is an orally bioavailable, potent tyrosine kinase inhibitor that is highly selective for HER2 without significant inhibition of EGFR. Inhibition of EGFR has been associated with significant toxicities, including skin rash and diarrhea. Tucatinib has shown activity as a single agent and in combination with both chemotherapy and other HER2 directed agents such as trastuzumab.¹ Studies of tucatinib in these combinations have shown activity both systemically and in brain metastases. HER2 is a growth factor receptor that is overexpressed in multiple cancers, including breast, ovarian and gastric cancers. HER2 mediates cell growth, differentiation and survival. Tumors that overexpress HER2 are more aggressive and historically have been associated with poor overall survival, compared with HER2-negative cancers.

About HER2-Positive Metastatic Breast Cancer

Patients with HER2-positive breast cancer have tumors with high levels of a protein called human epidermal growth factor receptor 2 (HER2), which promotes the aggressive spread of cancer cells. The American Cancer Society estimates that 20-25 percent of the approximately 234,000 annual breast cancer diagnoses in the U.S. are HER2-positive. Historically, HER2 disease has been associated with shorter survival times as well as a higher risk of recurrence and CNS disease (brain metastases). Approximately 30 to 50 percent of HER2-positive breast cancer patients develop brain metastases over time.^{2,3} Over the past two decades, the approvals of four targeted treatments (trastuzumab, pertuzumab, lapatinib, and ado-trastuzumab emtansine) have led to improved time to progression and survival rates of HER2-positive patients. Despite these advances, there is still a significant need for new therapies that can impact metastatic disease, including brain metastases, and be tolerated for longer periods of time.

About Cascadian Therapeutics

Cascadian Therapeutics is a clinical-stage biopharmaceutical company dedicated to developing innovative product candidates for the treatment of cancer. The lead product candidate, tucatinib (also known as ONT-380) is an oral, selective small molecule HER2 inhibitor. Cascadian Therapeutics is conducting a randomized, double-blind, placebo-controlled pivotal clinical trial called HER2CLIMB, which is evaluating tucatinib versus placebo in combination with capecitabine and trastuzumab in late stage HER2-positive breast cancer patients, with and without brain metastases, who have previously been treated with a taxane, trastuzumab, pertuzumab and T-DM1. Additional details on HER2CLIMB can be found at www.clinicaltrials.gov (Identifier: NCT02614794) or www.HER2CLIMB.com. For more information, please visit www.cascadianrx.com.

Forward-Looking Statements

In order to provide Cascadian Therapeutics' investors with an understanding of its current results and future prospects, this release contains statements that are forward-looking. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "will," "intends," "potential," "possible" and similar expressions are intended to identify forward-looking statements. These forward-looking statements include Cascadian Therapeutics' expectations regarding clinical development activities, and the potential benefits of tucatinib. Forward-looking statements involve risks and uncertainties related to Cascadian Therapeutics' business and the general economic environment, many of which are beyond its control. These risks, uncertainties and other factors could cause Cascadian Therapeutics' actual results to differ materially from those projected in forward-looking statements, including the risks associated with the costs and expenses of developing its product candidates, the adequacy of financing and cash, cash equivalents and investments, changes in general accounting policies, general economic factors, achievement of the results it anticipates from its preclinical development and clinical trials of its product candidates and its ability to adequately obtain and protect its intellectual property rights. Although

Cascadian Therapeutics believes that the forward-looking statements contained herein are reasonable, it can give no assurance that its expectations are correct. All forward-looking statements are expressly qualified in their entirety by this cautionary statement. For a detailed description of Cascadian Therapeutics' risks and uncertainties, you are encouraged to review the documents filed with the securities regulators in the United States on EDGAR and in Canada on SEDAR. Except as required by law, Cascadian Therapeutics does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

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References:

1. Koch et al. American Association of Clinical Research (AACR) 2011.
2. Metro et al. Clinical outcome of patients with brain metastases from HER2-positive breast cancer treated with lapatinib and capecitabine, *Annals of Oncology*, vol. 212, no. 3, pp. 625-630, 2011.
3. DOI: 10.1200/JCO.2013.54.0955 *Journal of Clinical Oncology*32, no. 19 (July 2014) 2100-2108.

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