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Prolonged Progression-Free Survival Reinforces Tucatinib's Potential for Patients with Advanced HER2+ Metastatic Breast Cancer

Subgroup Analysis from Two Ongoing Combination Studies of Tucatinib Demonstrates Prolonged PFS Benefit Regardless of Presence of Brain Metastases or Patient Characteristics

SAN ANTONIO, Dec. 07, 2017 (GLOBE NEWSWIRE) -- Cascadian Therapeutics, Inc. (NASDAQ:CASC), a clinical-stage biopharmaceutical company, today announced that tucatinib in combination with standard of care agents demonstrated prolonged progression-free survival (PFS) in a subgroup of patients participating in two ongoing Phase 1b studies. Results from a subgroup analysis from these tucatinib combination studies showed 22 percent of patients with HER2-positive (HER2+) metastatic breast cancer with and without brain metastases achieved prolonged PFS defined as twice the median PFS seen in these studies or else defined as survival greater than 17 months. Patients received a median of two prior HER2-based regimens and the median duration of the last prior treatment in this subgroup was 9.03 months. Patients with prolonged PFS on tucatinib combination therapy included those with characteristics that historically predict poor outcome such as hormone receptor status, presence of visceral disease, burden of systemic or brain disease and age. Results from this analysis will be presented in a poster session at the 2017 San Antonio Breast Cancer Symposium (SABCS) on Friday, December 8, 2017 beginning at 5:00 p.m. CST.

"One of the challenges in the treatment of HER2+ breast cancer is the frequent development of brain metastases, which occur in up to 50 percent of patients with advanced disease," said Erika Hamilton, M.D., Director of Breast and Gynecology Cancer Research and Principal Investigator at Sarah Cannon Research Institute. "Tucatinib in combination has shown early signs of activity in HER2+ brain metastases. An active agent showing prolonged activity systemically as well as in the brain, with a tolerable safety profile, would represent a meaningful advancement in treating metastatic breast cancer."

Dr. Hamilton continued, "The more mature dataset from these Phase 1b combination studies show tucatinib may be combined with other standard targeted therapies to achieve disease control in patients who have received multiple prior lines of therapy."

Prolonged Progression-Free Survival in Advanced HER2+ Metastatic Breast Cancer with or without Brain Metastases: A Pooled Analysis of Tucatinib Phase 1b Studies

In this poster, data from two Phase 1b combination studies of tucatinib were pooled to analyze the subgroup of patients with prolonged PFS, which was identified as patients achieving at least twice the observed median PFS in the overall group. Baseline characteristics and radiology findings were compared between the subgroup of patients with or without prolonged PFS from two studies: tucatinib in combination with trastuzumab (Herceptin®) and capecitabine (Xeloda®) in heavily pre-treated patients with advanced HER2+ breast cancer with or without brain metastases (ONT-380-005/Triplet study; n=27), and tucatinib in combination with T-DM1 (ONT-380-004; n=50). Of the 77 patients in the pooled analysis, 47 percent (n=36) of patients are without brain metastases and 53 percent (n=41) are with brain metastases, including patients with untreated or progressive brain metastases after radiation therapy. Twenty-two percent (17/77) of patients demonstrated prolonged PFS; 20 percent (n=10/50) from Study 004 and 26 percent (n=7/27) from Study 005/Triplet. Data from pooled tucatinib studies suggest a similar proportion of patients with brain metastases in the subgroup of patients with prolonged PFS compared to the overall patient population.

In addition, the following investigator-initiated trial in progress poster was presented at SABCS.

Phase 1b/2 Open-Label Single Arm Study to Evaluate Safety and Efficacy of Tucatinib in Combination with Letrozole and Palbociclib in Subjects with Hormone Receptor Positive and HER2 Positive Metastatic Breast Cancer (TULiP Trial)

The University of Colorado Cancer Center presented a trials in progress poster summarizing the study design for the ongoing TULiP trial in patients with hormone receptor positive and HER2-positive (HR+/HER2+) metastatic breast cancer. In this study, tucatinib, a highly selective inhibitor of HER2 tyrosine kinase, is combined with an aromatase inhibitor letrozole and CDK4/6 inhibitor palbociclib. The TULiP study is expecting to enroll 40 patients. It is currently opened for enrollment at

the University of Colorado Denver, and soon will be opened at five additional academic institutions (members of Academic Breast Cancer Research Consortium): North Western University, Chicago, IL; University of Texas Health and Science Center at San Antonio, TX; Stony Brook University, NY; University of Arizona, Tucson, AZ, and University of New Mexico, Albuquerque, NM. The Phase 1b part of the trial is expected to enroll 20 patients and will evaluate the tolerability of tucatinib given at maximum tolerated dose (300mg by mouth twice a day) with the standard doses of palbociclib and letrozole. The Phase 2 part of the trial is expected to enroll 20 additional patients to enable analysis of efficacy by overall response rate and progression-free survival. Because of documented activity of tucatinib in the CNS disease, the TULiP trial will include patients with brain metastases. For more information, visit ClinicalTrials.gov, Identifier: NCT03054363.

"Finding novel treatments for HR+/HER2+ breast cancers remains an area of unmet clinical need, because of intrinsic resistance of these tumors to both anti-hormonal treatments and HER2-targeted agents," said Elena Shagisultanova, MD, PhD, Assistant Professor at the University of Colorado Denver Cancer Center and Lead Principal Investigator of TULiP trial. "We are very excited about the TULiP trial. There is significant preclinical evidence on synergistic anti-tumor activity of CDK4/6 inhibitors and HER2-targeted agents. Tucatinib, palbociclib and letrozole have largely non-overlapping toxicity profiles and metabolic pathways. We believe that this triple combination of targeted agents will be well tolerated and highly patient centered, as an effective non-chemotherapy based regimen for treatment of patients with HR+/HER2+ metastatic breast cancer. We are grateful for the support we received from both Cascadian Therapeutics and Pfizer while working on this trial."

To access these poster presentations, please visit www.cascadianrx.com.

About Tucatinib

Tucatinib is an investigational, orally bioavailable, potent tyrosine kinase inhibitor that is highly selective for HER2 without inhibition of EGFR. Inhibition of EGFR has been associated with clinical 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.[1,2] 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 (HER2+) are more aggressive and historically have been associated with poor overall survival, compared with HER2-negative cancers.

About HER2CLIMB Pivotal Trial

HER2CLIMB is a randomized (2:1), double-blind, placebo-controlled pivotal clinical trial comparing tucatinib vs. placebo, each in combination with capecitabine and trastuzumab and without loperamide or budesonide prophylaxis, in patients with locally advanced or metastatic HER2+ breast cancer who have had prior treatment with trastuzumab, pertuzumab and ado-trastuzumab emtansine, also known as T-DM1. The primary endpoint is progression-free survival (PFS) based upon independent radiologic review. 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 patients in the United States, Canada, Western Europe and Australia. Additional information is available at www.HER2CLIMB.com.

About HER2+ Metastatic Breast Cancer

Patients with HER2+ 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 246,660 annual new cases of breast cancer diagnoses in the U.S. are HER2+. Historically, HER2 disease has been associated with shorter survival times as well as a higher risk of recurrence and CNS disease (brain metastases). Up to 50 percent of patients with HER2+ metastatic breast cancer experience brain metastases over time.[3] Over the past two decades, the approvals of four targeted treatments (trastuzumab, pertuzumab, lapatinib, and T-DM1) have led to improved time to progression and survival rates of patients with HER2+ breast cancer. 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. Its lead product candidate, tucatinib, is an investigational oral, selective small molecule HER2 inhibitor. Cascadian Therapeutics is conducting a randomized, double-blind, controlled pivotal clinical trial called HER2CLIMB, which is comparing tucatinib vs. placebo, each in combination with capecitabine and trastuzumab, in patients with locally advanced or metastatic HER2+ breast cancer with and without brain metastases, who have previously been treated with trastuzumab, pertuzumab and T-DM1. Additional details on HER2CLIMB can be found at

www.HER2CLIMB.com or www.ClinicalTrials.gov. 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, HER2CLIMB enrollment, and the potential benefits of its product candidates. 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, the receipt of regulatory approvals, and its ability to adequately obtain and protect its intellectual property rights, and other factors discussed under the caption "Risk Factors" in Cascadian Therapeutics' Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2017 filed with the Securities and Exchange Commission. Although Cascadian Therapeutics believes that the forward-looking statements contained herein are reasonable as of the date hereof, 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 should review the documents filed by Cascadian Therapeutics with the securities regulators in the United States on EDGAR and in Canada on SEDAR. Cascadian Therapeutics does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof, except to the extent required by law.

1 Moulder, S. et al., Phase 1 Study of ONT-380, a HER2 Inhibitor, in Patients with HER2+ Advanced Solid Tumors, with an Expansion Cohort in HER2+ Metastatic Breast Cancer. Clin Cancer Res. May 2017.
2 Hamilton, E. et al., Efficacy of a Phase 1b Study of Tucatinib (ONT-380), an Oral HER2-Specific Inhibitor, in Combination with Capecitabine and Trastuzumab in HER2+ Metastatic Breast Cancer, Including Patients with Brain Metastases. Presented at the SABCS Annual Meeting 2016. December 9, 2016 (Poster P4-21-01).
3 Ramakrishna N., et al., Journal of Clinical Oncology. 32, no. 19 (July 2014) 2100-2108.

Source: Cascadian Therapeutics, Inc.

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