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Cascadian Therapeutics' Lead Candidate, Tucatinib, Receives Orphan Drug Designation from FDA for Treatment of Breast Cancer Patients with Brain Metastases

SEATTLE, June 08, 2017 (GLOBE NEWSWIRE) -- Cascadian Therapeutics, Inc. (NASDAQ:CASC), a clinical-stage biopharmaceutical company, today announced that tucatinib, an investigational oral, small molecule kinase inhibitor that is highly selective for HER2 and the Company's lead product in development, has been granted orphan drug designation by the U.S. Food and Drug Administration ("FDA") for the treatment of breast cancer patients with brain metastases.

"Brain metastases arise in up to 50 percent of women with HER2-positive metastatic breast cancer and these metastases can compromise quality of life and survival," explained Eric P. Winer, MD, of Boston's Dana-Farber Cancer Institute.

Winer's colleague, Nancy U. Lin, MD, added, "Treatments for patients with brain metastases have been limited, and we urgently need new and more effective approaches."

"There remains an unmet medical need for patients with HER2-positive metastatic breast cancer, including patients whose disease has metastasized to the brain," said Scott Myers, President and CEO of Cascadian Therapeutics. "New treatment options are clearly needed and tucatinib is being developed to fit within the current and emerging treatment paradigm. Our ongoing registrational trial of tucatinib known as HER2CLIMB is enrolling patients with all types of brain metastases, including untreated, previously treated stable or progressing brain metastases. Approximately half of patients enrolled in HER2CLIMB to date have had brain metastases at study entry, which will allow us to assess activity in that subpopulation in a statistically meaningful way. We are encouraged by results from our ongoing Phase 1b combination study of tucatinib plus capecitabine and/or trastuzumab, which showed a 42 percent response rate in patients with HER2-positive brain metastases."

The FDA's Orphan Drug Designation program provides orphan status to drugs defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases that affect fewer than 200,000 people in the U.S. Orphan designation qualifies the sponsor of the drug for certain development incentives, including tax credits for qualified clinical testing, prescription drug user fee exemption and 7-year marketing exclusivity upon FDA approval.

About Tucatinib

Tucatinib is an investigational, 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.[1,2] 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 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 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 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 and Canada. Clinical sites in Western Europe, Australia and Israel are expected to open in the first half of 2017.

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 246,660 annual new cases of 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.[3,4] 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-positive 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. The lead product candidate, tucatinib (also known as ONT-380), is an investigational oral, selective small molecule HER2 inhibitor. Cascadian Therapeutics is conducting a randomized, double-blind, placebo-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-positive breast cancer 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.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, timing of additional data, 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. 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.

References:
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 San Antonio Breast Cancer Symposium (SABCS) Annual Meeting 2016, San Antonio, TX, December 9, 2016 (Poster P4-21-01).
3. 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.
4. Ramakrishna N., et al., Journal of Clinical Oncology 32, no. 19 (July 2014) 2100-2108.

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