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Tucatinib Data in Multiple Tumor Types Presented at the European Society for Medical Oncology (ESMO) 2017 Congress

Results from Pooled Analysis Support the Potential Utility of Tucatinib for Patients with HER2+ Metastatic Breast Cancer with Brain Metastases

Data from Nonclinical Models Support Evaluation of Tucatinib in HER2+ Gastrointestinal Cancers

SEATTLE, Sept. 11, 2017 (GLOBE NEWSWIRE) -- Cascadian Therapeutics, Inc. (NASDAQ:CASC), a clinical-stage biopharmaceutical company, today announced tucatinib data in multiple tumor types were presented at the European Society for Medical Oncology (ESMO) 2017 Congress being held September 8-12, 2017 in Madrid, Spain. Results from the pooled analysis of Phase 1b combination studies support the potential utility of tucatinib for patients with HER2-positive (HER2+) metastatic breast cancer with brain metastases, including untreated or progressive brain metastases after radiation therapy. HER2 disease has been associated with shorter survival times as well as a higher risk of recurrence and brain metastases.

"Approximately 30-to-50 percent of patients with metastatic HER2+ breast cancer will develop brain metastases over time and, historically, patients with HER2+ brain metastases have had poorer outcomes compared to those without," said Stacy L. Moulder, MD, Associate Professor, Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX. "The results from this pooled analysis of tucatinib combination studies suggesting that patients with HER2+ brain metastases, including those with untreated or progressing disease, have similar progression-free survival compared to those without brain metastases is promising and supports inclusion of patients with brain metastases into ongoing clinical trials. There remains a clinical need for safe and effective HER2-targeted therapies that are active both systemically and in the brain."

Luke Walker, MD, Senior Vice President, Clinical Development of Cascadian Therapeutics, added, "These data from our Phase 1b trials further support the inclusion of patients with brain metastases in our ongoing registrational trial of tucatinib in combination with capecitabine and trastuzumab. This trial, known as HER2CLIMB, is enrolling patients with all types of brain metastases, including untreated, previously treated 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."

Progression-free survival (PFS) and site of first progression in HER2+ metastatic breast cancer patients with or without brain metastases: A pooled analysis of tucatinib phase I studies (Poster 264)

In this poster (264), data from two Phase 1b combination studies of tucatinib were pooled to analyze baseline characteristics and outcomes of patients with and without brain metastases: 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), and tucatinib in combination with T-DM1 (ONT-380-004). Of the 77 patients in the pooled analysis, 47 percent (n=36) of patients are without brain metastases and 53 percent (n=41) with brain metastases, including patients with untreated or progressive brain metastases after radiation therapy. Four subgroups were identified retrospectively based on historical data and then compared with respect to baseline characteristics, progression-free survival and site of progression. Data from pooled tucatinib studies suggest the PFS of patients with and without brain metastases were similar, regardless of whether brain metastases were untreated or progressed after radiation therapy.

In addition, the following nonclinical poster supports the clinical evaluation of tucatinib for the treatment of other HER2+ tumor types.

Tucatinib, a HER2 selective kinase inhibitor, is active in patient derived xenograft (PDX) models of HER2-amplified colorectal, esophageal and gastric cancer (Poster 1639)

In this poster, data are presented that show tucatinib is active as a single agent in nonclinical models of HER2+ gastrointestinal cancers, including colorectal, esophageal and gastric cancers. The data also demonstrate that tucatinib

combined with trastuzumab displayed superior anti-tumor activity compared with either single agent, producing a higher proportion of partial and complete tumor regressions. These nonclinical data support the clinical evaluation of tucatinib for the treatment of HER2+ gastrointestinal cancers. Tucatinib is currently being evaluated in an open label Phase 2 study combining tucatinib with trastuzumab in HER2+/RAS wild type metastatic colorectal cancer (MOUNTAINEER: NCT03043313).

Scott Peterson, Ph.D., Chief Scientific Officer of Cascadian Therapeutics, commented, "We are pleased to share this update regarding the potential versatility of tucatinib in combination for other tumor types beyond breast cancer."

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. 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.

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