Oncternal Therapeutics Announces Presentation of Interim Clinical Data on Cirmtuzumab in Combination with Paclitaxel at 2019 San Antonio Breast Cancer Symposium

December 12, 2019

- Four of seven evaluable patients with HER2-negative, metastatic or locally-advanced unresectable breast cancer achieved a partial response for an objective response rate of 57%

- Cirmtuzumab in combination with paclitaxel has been well tolerated

SAN DIEGO--(BUSINESS WIRE)--Dec. 12, 2019-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced the presentation of interim data from the ongoing, investigator-sponsored Phase 1b clinical study of cirmtuzumab, its investigational anti-ROR1 monoclonal antibody, in combination with paclitaxel in patients with HER2-negative, metastatic or locally-advanced unresectable breast cancer. The results were presented at the San Antonio Breast Cancer Symposium (SABCS) in San Antonio, TX. A copy of the poster presentation is available online at www.oncternal.com.

As of the data cut-off date of November 27, 2019, a total of eight patients with HER2-negative, metastatic or locally-advanced unresectable breast cancer were enrolled in the study. Seven of the eight patients were evaluable for safety and efficacy. Four of the patients had triple negative breast cancer (TNBC) at study enrollment.

Four of the seven evaluable patients achieved a partial response, for an objective response rate of 57%, including one partial response that continued on cirmtuzumab alone for 30 weeks after discontinuing paclitaxel.

The combination of cirmtuzumab and paclitaxel has been well tolerated in this trial, with no study discontinuations for toxicity and no dose-limiting toxicities observed to date. Adverse events have been consistent with the known safety profile of paclitaxel alone.

Pharmacokinetic analysis of serial plasma samples for free unbound antibody from two patients provided results similar to those observed in previous studies of chronic lymphocytic leukemia patients, consistent with a projected half-life of 30 days. No decline in antibody concentration over time was observed, consistent with the absence of neutralizing antibodies.

“It is encouraging to see that cirmtuzumab in combination with paclitaxel has been well tolerated and is active. Future studies will determine whether cirmtuzumab is contributing to the known activity of paclitaxel. Advanced breast cancer patients are in need of improved treatment options with acceptable side effects. We look forward to completing enrollment and treating additional patients in this study,” said Rebecca Shatsky, M.D., Assistant Clinical Professor, Medicine at University of California San Diego School of Medicine, lead investigator who presented the poster.

Funding for this trial was provided by Oncternal Therapeutics, California Institute for Regenerative Medicine, UC San Diego Alpha Stem Cell Clinic and Sanford Stem Cell Clinical Center, UC San Diego Moores Cancer Center, Padres Pedal the Cause Grant, and Gonick Breast Cancer Research Funds.

“The early activity signals for cirmtuzumab in combination with paclitaxel for patients with breast cancer seen in this study are encouraging. We believe these data, taken together with the previously updated clinical data in chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL) from the CIRLL study presented at the annual ASH meeting, reinforce the encouraging safety data and provide evidence of clinical activity of cirmtuzumab and its potential for the treatment of patients with breast cancer and other ROR1-expressing solid tumors and hematological malignancies,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO.

About the Clinical Trial

This clinical trial is an investigator-sponsored Phase 1b Pilot Clinical Trial of Cirmtuzumab, an Anti-ROR1 Monoclonal Antibody, in Combination with Paclitaxel for the Treatment of Patients with Metastatic, or Locally Advanced, Unresectable Breast Cancer. The objectives of the trial include the evaluation of safety, tolerability, pharmacokinetics, and clinical activity. Eligible patients are those with locally-advanced, unresectable or metastatic HER2-negative breast cancer who had not received paclitaxel in the metastatic setting. Study treatment included a fixed dose of 600 mg cirmtuzumab given on days 1 and 15 of cycle 1, and then on day 1 of each subsequent 28-day cycle. Paclitaxel was given weekly at a dose of 80 mg/m^2. Additional information about the clinical trial may be accessed at ClinicalTrials.gov (NCT02776917).

About Cirmtuzumab

Cirmtuzumab is an investigational, potentially first-in-class monoclonal antibody targeting ROR1, or Receptor tyrosine kinase-like Orphan Receptor 1. Cirmtuzumab is currently being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of CLL or MCL, in a collaboration with the UC San Diego School of Medicine and the California Institute for Regenerative Medicine (CIRM). In addition, an investigator-initiated Phase 1 clinical trial of cirmtuzumab in combination with paclitaxel for women with metastatic breast cancer is being conducted at the UC San Diego School of Medicine. CIRM has also provided funding to support development programs for cirmtuzumab and a CAR-T therapy that targets ROR1, which is currently in preclinical development as a potential treatment for hematologic cancers and solid tumors.

ROR1 is a potentially attractive target for cancer therapy because it is an oncofetal antigen – a protein that confers a survival and fitness advantage when reactivated and expressed by tumor cells. When expressed by hematologic malignancies such as CLL and MCL, ROR1 acts as a receptor for the tumor growth factor Wnt5a. Researchers at the UC San Diego School of Medicine discovered that targeting a critical epitope on ROR1 was key to inhibiting Wnt5a activation, specifically targeting ROR1 expressing tumors. This led to the development of cirmtuzumab that binds this critical epitope of ROR1, which is highly expressed on many different cancers but not on normal tissues. Preclinical data showed that when cirmtuzumab bound to

ROR1, it blocked Wnt5a signaling, inhibited tumor cell proliferation, migration and survival, and induced differentiation of the tumor cells. Cirmtuzumab is in clinical development and has not been approved by the U.S. Food and Drug Administration for any indication.

About Oncternal Therapeutics

Oncternal Therapeutics is a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies for the treatment of cancers with critical unmet medical need. Oncternal focuses drug development on promising yet untapped biological pathways implicated in cancer generation or progression. The pipeline includes cirmtuzumab, an investigational monoclonal antibody designed to inhibit the ROR1 pathway, a type I tyrosine kinase-like orphan receptor, that is being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL), and TK216, an investigational targeted small-molecule inhibitor of the ETS family of oncoproteins, that is being evaluated in a Phase 1 clinical trial for patients with Ewing sarcoma alone and in combination with vincristine chemotherapy. In addition, Oncternal has a program to develop a CAR-T therapy that targets ROR1, which is currently in preclinical development as a potential treatment for hematologic cancers and solid tumors. More information is available at www.oncternal.com.

Forward-Looking Information

Oncternal cautions you that statements included in this press release that are not a description of historical facts are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negatives of these terms or other similar expressions. These statements are based on the company’s current beliefs and expectations. Forward looking statements include statements regarding Oncternal’s beliefs, goals, intentions and expectations, and include: the potential of cirmtuzumab to treat ROR1 expressing cancers, including CLL, MCL, HER2-negative breast cancer and other solid tumors, and the potential for interim data results to be replicated as the ongoing trial continues; statements regarding Oncternal’s clinical development plans; and Oncternal’s belief that ROR1 is a potentially attractive target for cancer therapy. Forward looking statements are subject to risks and uncertainties inherent in Oncternal’s business, which include, but are not limited to: the risk that interim results of a clinical trial do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available, including interim response results may not be confirmed by later assessments; the risk that unforeseen adverse reactions or side effects may occur in the course of developing and testing product candidates such as cirmtuzumab and Oncternal’s other product candidates, which could adversely impact the company’s ability to complete clinical trials and obtain regulatory approval for such product candidates; uncertainties associated with the clinical development and process for obtaining regulatory approval of cirmtuzumab and Oncternal’s other product candidates, including potential delays in the commencement, enrollment and completion of clinical trials; Oncternal’s dependence on the success of cirmtuzumab and its other product development programs; the risk that the regulatory landscape that applies to the development program for cirmtuzumab and the company’s other product candidates may change, which could result in delays or termination of development of such product candidates or unexpected costs in obtaining regulatory approvals; the risk that competitors may develop technologies or product candidates more rapidly than Oncternal, or that are more effective than Oncternal’s product candidates, which could significantly jeopardize Oncternal’s ability to develop and successfully commercialize its product candidates; Oncternal’s limited operating history and the fact that it has incurred significant losses, and expects to continue to incur significant losses for the foreseeable future; the risk that the company may not be able to obtain sufficient additional financing when needed or at all as required to achieve its goals, which could force the company to delay, limit, reduce or terminate its product development programs or other operations, and other risks described in the company’s prior press releases as well as in public periodic filings with the U.S. Securities & Exchange Commission. All forward-looking statements in this press release are current only as of the date hereof and, except as required by applicable law, Oncternal undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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