Oncternal Therapeutics Announces Presentation of Clinical Data Update on Cirmtuzumab in Combination with Ibrutinib at 2019 ASH Annual Meeting

December 9, 2019

- *Interim data show that patients with CLL achieved overall best objective response rate of 85% with progression-free survival of 100%*
- *Cirmtuzumab has been very well tolerated in this trial*
- *Inhibition of ROR1 signaling by cirmtuzumab was shown to reverse gene expression signatures associated with cancer-cell-stemness, oncogenic dedifferentiation, and inflammation*

SAN DIEGO--(BUSINESS WIRE)--Dec. 9, 2019-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced the presentation of updated interim clinical data from the ongoing Phase 1/2 CIRLL (Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma) clinical trial, in which cirmtuzumab, an investigational anti-ROR1 monoclonal antibody, is being evaluated in combination with ibrutinib in patients with chronic lymphocytic leukemia (CLL) or mantle cell lymphoma (MCL). The results were presented at the American Society of Hematology (ASH) Annual Meeting in Orlando. A copy of the poster presentation is available online at www.oncternal.com.

Thirty-four patients with CLL who had never been treated with a BTK inhibitor were enrolled in the dose-finding and dose-confirming cohorts of this clinical trial, including 12 treatment-naïve and 22 relapsed/refractory patients, and all 34 were evaluable for efficacy. As of the data cut-off in early November 2019,

- Twenty-nine of the 34 patients achieved a response, for an overall best objective response rate of 85%.
- One patient achieved a complete response (CR) and remained in remission six months after completion of the trial and discontinuation of all anti-CLL therapy. In addition, three patients met radiographic and hematologic response criteria for Clinical CR, bone marrow biopsy not performed but pending.
- Five patients had stable disease.
- The total clinical benefit rate was 100%.
- None of the patients progressed or died, for a progression-free survival (PFS) of 100% with a median follow-up of 7.4 months.
- Patients achieved responses rapidly, with 68% of patients achieving a clinical response by three months on combination therapy.
- The rise in leukemic cell counts that is typically seen in the first six months with ibrutinib monotherapy was blunted with the cirmtuzumab plus ibrutinib combination, and leukemic cell counts returned toward baseline and normal levels rapidly.

Twelve patients with relapsed/refractory MCL, eight of whom were evaluable for efficacy, were enrolled in the dose-finding cohort of this trial. As of the data cut-off, five of the eight evaluable patients had achieved a clinical response, for an overall best objective response rate of 63% at a median follow-up of six months. Two patients with aggressive or bulky and heavily pre-treated MCL achieved CR, the longest of which is continuing with the patient on study for over 17 months. In addition, three patients had stable disease, for a total clinical benefit rate of 100%.

Cirmtuzumab as a single agent has been very well tolerated in this study. The combination of cirmtuzumab plus ibrutinib has also been well tolerated, with adverse events consistent with those reported for ibrutinib alone. There have been no dose limiting toxicities and no serious adverse events attributed to cirmtuzumab alone.

Genetic analysis of CLL cells from three patients showed pre-treatment transcriptome profiles associated with a stemness signature and NF-kB-driven inflammation. Both genetic signatures were reversed in these patients following cirmtuzumab treatment.

“It is exciting to see that cirmtuzumab in combination with ibrutinib continues to be well tolerated and has demonstrated 100% progression-free survival in patients with CLL, as well as encouraging early signals of efficacy in patients with MCL,” said Michael Choi, M.D., Associate Clinical Professor of Medicine in the Division of Hematology-Oncology at University of California San Diego School of Medicine, who is the lead investigator for the CIRLL clinical trial.

The CIRLL clinical trial is supported by a grant from the California Institute for Regenerative Medicine (CIRM) and is being conducted in collaboration with the UC San Diego School of Medicine.

“We are encouraged by the evidence of clinical activity and the safety data demonstrated by cirmtuzumab in the ongoing CIRLL clinical trial. We continue to be excited about its potential for the treatment of patients with ROR1-expressing cancers, including CLL, MCL, Her2-negative breast cancer and other solid tumors,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO.

About the CIRLL Clinical Trial

The CIRLL clinical trial (CIRM-0001) is a Phase 1/2 trial evaluating cirmtuzumab in combination with ibrutinib in separate groups of patients with

chronic lymphocytic leukemia (CLL) or mantle cell lymphoma (MCL). Part 1 of the clinical trial was a Phase 1 dose-finding cohort designed to determine the Phase 2 dose, or recommended dosing regimen (RDR). Part 2 is a Phase 1b expansion cohort to confirm the RDR. Part 3 of the study, which is now open for enrollment, is a Phase 2 study in which approximately 90 patients with CLL will be randomized to receive either ibrutinib alone or ibrutinib plus cirmtuzumab, with a primary endpoint of complete response rate. Additional information about the CIRM-0001 clinical trial and other clinical trials of cirmtuzumab may be accessed at ClinicalTrials.gov.

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 and MCL, in a collaboration with the University of California 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 or continue to show improved clinical efficacy 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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