Oncternal Therapeutics Announces Opening of Phase 1b Expansion Cohort of Clinical Trial of Cirmtuzumab in Combination with Ibrutinib in Patients with Mantle Cell Lymphoma

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Cirmtuzumab combination demonstrated clinical activity with complete responses in mantle cell lymphoma

SAN DIEGO--(BUSINESS WIRE)--Oct. 3, 2019-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced that it has opened for enrollment a Phase 1b expansion cohort of its Phase 1/2 clinical trial of cirmtuzumab, a ROR1-targeted monoclonal antibody, combined with ibrutinib, in patients with mantle cell lymphoma (MCL). The decision to open an expansion cohort in MCL of the ongoing Phase 1/2 CIRLL (Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma) clinical trial was based on favorable interim results from the dose-finding cohort of the trial, including that the combination was well-tolerated and that complete responses were observed in two heavily pre-treated patients who had received and failed multiple chemotherapy regimens and an autologous transplant, as well as either an allotransplant or CAR-T therapy, prior to participating in this clinical trial.

In June, the Company presented interim data at the American Society of Clinical Oncology (ASCO) annual meeting, including the preliminary results from the first six patients with MCL treated in the CIRLL clinical trial. One patient with MCL, who had relapsed following an allogeneic stem cell transplant, experienced a confirmed complete response (CR) after three months of cirmtuzumab plus ibrutinib treatment, including complete resolution of a large mediastinal mass. This CR appears to be sustained and has been confirmed to be ongoing after completing 12 months of cirmtuzumab plus ibrutinib treatment. Following ASCO, a second confirmed CR occurred in a patient who had progressive disease after failing several different chemotherapy regimens, autologous transplant and CAR-T therapy. Additional data from this clinical trial will be presented at a future medical conference.

“It is encouraging to see that the drug has been well tolerated as well as the early signal of efficacy of cirmtuzumab with ibrutinib in MCL, particularly the rapid and durable complete responses of the heavily pre-treated patients after three months of therapy, which is an unusually fast response in this patient population,” said Hun Lee, M.D., Assistant Professor of Medicine in the Department of Lymphoma & Myeloma at the University of Texas MD Anderson Cancer Center, who is an investigator on 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 University of California San Diego (UC San Diego).

“We are pleased to be opening the expansion cohort portion of the CIRLL clinical trial for patients with MCL, and continue to be encouraged by the interim results from this study for both patients with MCL and patients with chronic lymphocytic leukemia, for whom a randomized Phase 2 portion of the trial was opened in August,” 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 portion designed to determine the Phase 2 dose, or recommended dosing regimen (RDR). Part 2 is a Phase 1b expansion cohort to confirm the RDR. 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 developing product candidates 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 receptor, 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 small-molecule compound that is designed to inhibit E26 transformation specific (ETS) family 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 plans to present additional data from its ongoing Phase 1/2 clinical trial of cirmtuzumab; the expectation that Oncternal will be able to enroll patients into the Phase 1b expansion cohort; and Oncternal’s belief that favorable outcomes from the ongoing Phase 1 portion of the clinical trial support opening the Phase 1b portion. The inclusion of forward-looking statements should not be regarded as a representation by Oncternal that any of its plans will be achieved. Actual results may differ from those set forth in this release due to the risks and uncertainties inherent in Oncternal’s business, including, without limitation: 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; the Company’s dependence on the success of cirmtuzumab and its other product development programs; 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; 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; the Company’s limited operating history and that fact that it has incurred significant losses, and expects to continue to incur significant losses for the foreseeable future; risks related to the inability of Oncternal to obtain sufficient additional capital to continue to advance the development of cirmtuzumab and its other product candidates; 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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