Oncternal Therapeutics Announces Increased Focus of the Cirmtuzumab ROR1 Antibody Program on Mantle Cell Lymphoma

June 30, 2020

- Increasing planned enrollment of patients with MCL in ongoing CIRLL Phase 1/2 clinical trial of cirmtuzumab with ibrutinib based on encouraging data presented at ASCO 2020

- Meeting requested with FDA to discuss registration pathway for cirmtuzumab for patients with MCL

SAN DIEGO--(BUSINESS WIRE)--Jun. 30, 2020-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced an updated clinical strategy for its investigational ROR1 monoclonal antibody, cirmtuzumab, that prioritizes development in mantle cell lymphoma (MCL), based on encouraging interim clinical results from the ongoing Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma (CIRLL) Phase 1/2 clinical trial that were presented at the American Society of Clinical Oncology 2020 Annual Meeting (ASCO 2020) in May 2020.

The Company reported a 58% complete response (CR) rate, a 83% overall best objective response rate (ORR), and a progression free survival rate of 17.5 months with a median follow-up of 8.3 months, for patients with relapsed/refractory MCL in the ongoing Phase 1/2 CIRLL clinical trial of cirmtuzumab in combination with ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, at ASCO 2020. These response rates in heavily pre-treated patients were higher than the historical published CR of 23% and ORR of 67% for single-agent ibrutinib for patients with MCL who had received more than one prior therapy (Rule 2019, Haematologica). Four of these patients with MCL had been previously treated with and responded to ibrutinib, prior to participating in the CIRLL study. All four of these patients responded to the combination of cirmtuzumab and ibrutinib, two achieving CRs and two achieving partial responses. The Company believes that the interim results presented at ASCO 2020 are clinically relevant given the unmet medical need for patients with MCL.

As a result, the Company is amending the CIRLL study to increase the number of patients with relapsed/refractory MCL to be enrolled in the Phase 2 Expansion Cohort to at least 20 patients and to allow enrollment of patients with a broader range of prior BTK inhibitor treatments.

The Company has also requested a meeting with the U.S. Food and Drug Administration (FDA) to discuss the results of the recent interim analysis of the CIRLL study and to seek guidance on a potential accelerated approval pathway for cirmtuzumab plus ibrutinib in patients with relapsed/refractory MCL.

At ASCO 2020, the Company also reported a 100% progression-free survival rate, 88% ORR and 3% CR rate, with a median follow-up of 12.8 months, for patients with chronic lymphocytic leukemia (CLL) treated with cirmtuzumab in combination with ibrutinib in the CIRLL study. These interim data did not satisfy the hypothesis that ibrutinib plus cirmtuzumab would produce a CR rate 25% greater than the historical response rate for ibrutinib alone. Based on these interim results, Oncternal will continue treatment and follow-up of the patients with CLL who are already enrolled in the CIRLL study for up to two years or until disease progression, but will limit total enrollment of patients in the randomized Phase 2 CLL cohort to approximately 35 patients, in order to focus resources on the MCL portion of the study. The Company believes that, while significant unmet medical need exists in both CLL and MCL, the MCL indication may offer a more rapid path to potential regulatory approval.

Additionally, Oncternal plans to further explore clinical combination strategies for cirmtuzumab for patients with hematologic malignancies. Accordingly, the Company is supporting a new, investigator-sponsored Phase 2 clinical trial of cirmtuzumab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL in collaboration with the University of California San Diego School of Medicine (UC San Diego). Preclinical studies performed in the laboratory of Dr. Thomas Kipps at UC San Diego reported synergy between cirmtuzumab and venetoclax, providing a rationale for this combination clinical trial (Rassenti 2017, PNAS).

"We are excited about the promising clinical data reported for cirmtuzumab in combination with ibrutinib for patients with relapsed/refractory MCL, for whom a significant unmet medical need exists for well-tolerated therapies that provide more complete and durable responses. We plan to prioritize the development of cirmtuzumab for patients with MCL and expect that the planned changes will accelerate the Company's timetable for initiating a potential registrational study for cirmtuzumab, while having an overall favorable budget impact," said James Breitmeyer, M.D., Ph.D., Oncternal's President and CEO. "Additionally, we are pleased to support a new, investigator-sponsored Phase 2 clinical trial of cirmtuzumab in combination with venetoclax for the treatment of patients with CLL, based on promising published preclinical data. Our collaborators at UC San Diego and the California Institute for Regenerative Medicine (CIRM) have indicated that they support our revised development strategy for cirmtuzumab."

About the CIRLL Clinical Trial

The CIRLL clinical trial (Cirmtuzumab and Ibrutinib for Relapsed Lymphoma and Leukemia, Study CIRM-0001) is a Phase 1/2 trial evaluating cirmtuzumab in combination with ibrutinib in separate groups of patients with MCL or CLL. Enrollment has been completed in the dose-finding cohorts in CLL and MCL, and the dose-expansion cohort in CLL. Based on the data from the dose-finding cohorts, the recommended dosing regimen was determined to be 600 mg of cirmtuzumab administered intravenously every two weeks for three doses, followed by dosing every four weeks, in combination with 560 mg of ibrutinib once daily for patients with MCL, or 420 mg of ibrutinib administered once daily for patients with CLL, which are the FDA-approved doses of ibrutinib in these indications.

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 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.

ROR1 is a potentially attractive target for cancer therapy because it is an onco-embryonic antigen – not usually expressed on adult cells, and its expression confers a survival and fitness advantage when reactivated and expressed by tumor cells. Researchers at the UC San Diego School of Medicine discovered that targeting a critical epitope on ROR1 was key to 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 FDA 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 clinical 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 patients with chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL) and in an investigator-sponsored, Phase 1b clinical trial in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer, 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 MCL, CLL, Her2-negative breast cancer and other solid tumors, and benefit patients with unmet medical needs; Oncternal’s intention to expand enrolment patients with elapsed/refractory MCL; and the potential benefits of the investigator-sponsored Phase 2 clinical trial of cirmtuzumab in combination with venetoclax. Forward looking statements are subject to risks and uncertainties inherent in Oncternal’s business, which include, but are not limited to: the risk that preclinical studies and 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, which could adversely impact the company’s ability to complete clinical trials and obtain regulatory approval for such product candidates; Oncternal has encountered delays, and may encounter additional delays or difficulties, in enrolling patients in its clinical trials as a result of the COVID-19 pandemic; the COVID-19 pandemic may disrupt Oncternal’s business operations, increasing its costs; 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 risk that, if an orphan designated product, including cirmtuzumab, receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity; Oncternal’s dependence on the success of cirmtuzumab and its other product development programs; the risk that the approval of one of our product candidates may be blocked for seven years if a competitor obtains approval of the same drug or biologic, as defined by the FDA, or if our product candidate is determined to be contained within the competitor’s product for the same indication or disease, 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 will have insufficient funds to finances its operations after the fourth quarter of 2020 and 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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