Oncternal Therapeutics Announces Presentation of Update on Phase 1/2 Clinical Trial of Cirmtuzumab in Combination with Ibrutinib at 2020 ASCO Annual Meeting

May 19, 2020

- *58% complete response rate reported for patients with relapsed/refractory MCL, with a median follow-up of 8.3 months*
- *100% progression-free survival reported for patients with CLL, with a median follow-up of 12.8 months*
- *Cirmtuzumab continued to be well tolerated in this trial*

SAN DIEGO--(BUSINESS WIRE)--May 19, 2020-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced 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 mantle cell lymphoma (MCL) or chronic lymphocytic leukemia (CLL). The data will be presented as part of the American Society of Clinical Oncology (ASCO) 2020 Virtual Annual Meeting, and a copy of the poster presentation will be available online at www.oncternal.com on May 29, 2020:

- Abstract Title: Clinical activity of cirmtuzumab, an anti-ROR1 antibody, in combination with ibrutinib: Interim results of a phase 1/2 study in mantle cell lymphoma (MCL) or chronic lymphocytic leukemia (CLL) (abstract # 8036)
- Session Title: Hematologic Malignancies – Lymphoma and Chronic Lymphocytic Leukemia
- Session Date and Time: May 29, 2020, 8:00 – 11:00 CDT

“The reported 58% complete response rate for patients with relapsed/refractory MCL treated with cirmtuzumab and ibrutinib is highly encouraging and is higher than previously reported for ibrutinib alone in a similar patient population. Patients with relapsed MCL remain in dire need of well-tolerated treatment options that provide deeper and more durable responses,” said Hun Ju Lee, M.D., Associate 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 and the first author on the ASCO poster presentation.

“We are particularly encouraged by the improvement in the complete response rate for patients with relapsed/refractory MCL treated with the combination of cirmtuzumab and ibrutinib in our clinical trial, which is now 58%, as compared to the 25% complete response rate that we reported at the American Society of Hematology (ASH) meeting in December,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “We continue to be excited about cirmtuzumab’s potential for the treatment of patients with ROR1-expressing cancers, including MCL, CLL, Her2-negative breast cancer, and other solid tumors.”

As of the data cut-off date of April 30, 2020, 15 patients with relapsed/refractory MCL were enrolled in the dose-finding and dose-confirming cohorts of this clinical trial, 12 of whom were evaluable for efficacy:

- Seven of the 12 evaluable patients achieved a complete response, for a complete response (CR) rate of 58%, determined by Cheson criteria. One of the seven patients had a complete metabolic response (CMR) by PET scan, with an indeterminant bone marrow biopsy. Responses developed rapidly in most patients, with four of the seven CRs documented after approximately three months on the combination of cirmtuzumab and ibrutinib. All seven CRs were ongoing, including one patient who has remained in CR at over 23 months on study.
- The overall best objective response rate (ORR) was 83%, including patients who achieved a CR and three patients (25%) who achieved a partial response (PR). In addition, two patients had stable disease (SD), for a total best clinical benefit rate (including CR, PR and SD) of 100%.
- Median progression-free survival (PFS) was 17.5 months, with a median follow-up of 8.3 months.
- Patients had received an average of 2.8 prior therapies (range 1-5) before participating in this clinical trial, including four patients who had received prior treatment with ibrutinib. Seven of the 12 evaluable patients had high or intermediate Mantle Cell Lymphoma International Prognostic Index (MIPI) risk score at study entry.
- Historical data published for single-agent ibrutinib for patients with MCL, who had received more than one prior therapy, reported an ORR of 63%, CR rate of 23% and median PFS of 10.3 months (Rule 2019 Haematologica).

As of the data cut-off date on April 30, 2020, 34 patients with CLL were enrolled in the dose-finding and dose-confirming cohorts of this clinical trial, all of whom were evaluable for efficacy:

- Thirty of the 34 evaluable patients achieved a clinical response, for an overall best objective response rate of 88%, including one patient (3%) who achieved a CR, and 29 patients (85%) who achieved a PR. In addition, four patients had stable disease, for a total clinical benefit rate (including CR, PR, SD) of 100%.
- No patients progressed while in the study, and PFS was 100%, with a median follow-up of 12.8 months.
- Twelve patients were treatment-naïve and 22 had relapsed/refractory CLL. Patients with relapsed/refractory CLL had

received an average of 2.6 prior therapies (range 1-9) before participating in this clinical trial.

Cirmtuzumab as a single agent has been 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. Neutropenia of any grade occurred in six subjects (8.6%).

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 CLL or MCL. Enrollment of the dose-finding cohorts in CLL and MCL and dose-expansion cohort in CLL has been completed. Enrollment of the dose-expansion cohort in MCL and randomized Phase 2 cohort in CLL is ongoing. 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 420 mg of ibrutinib administered once daily for patients with CLL, or 560 mg of ibrutinib once daily for patients with MCL, which are the FDA-approved doses of ibrutinib in these indications. 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 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.

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 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 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 the potential for interim data results to be replicated or continue to show improved clinical efficacy as the ongoing trial continues. 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; 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; 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; comparisons to historical ibrutinib data are based on unrelated clinical trials and does not reflect results that might have been obtained from head-to-head studies, including due to differences in study protocols, conditions and patient populations; 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 will have insufficient funds to finances its operations after the third 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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