



## **Oncternal Therapeutics Announces Interim Clinical Data Update, Including 50% Complete Response Rate, for Cirmtuzumab in Combination with Ibrutinib in Patients with Mantle Cell Lymphoma**

March 11, 2020

- *50% (six of twelve) evaluable patients with relapsed/refractory MCL achieved complete responses (CR) in the dose-finding cohort of the ongoing Phase 1/2 clinical trial*
- *83% best objective response rate (ORR) and 100% clinical benefit rate*

SAN DIEGO--(BUSINESS WIRE)-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced an interim clinical data update for cirmtuzumab, a ROR1-targeted monoclonal antibody, combined with ibrutinib, in patients with relapsed/refractory mantle cell lymphoma (MCL) as part of the ongoing Phase 1/2 CIRLL (Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma) clinical trial (data cutoff as of March 6, 2020):

- 50% Complete Response (CR) rate (6 of 12 evaluable patients), determined by Cheson criteria. One of the six patients had a complete metabolic response (CMR) by PET scan, with a bone marrow biopsy pending. All six CRs are ongoing, including one patient who has remained in CR at over 21 months on study. Four of the six patients achieved CRs within four months on the combination of cirmtuzumab and ibrutinib
- 33% Partial Response (PR) rate (4 of 12)
- 17% Stable Disease (SD) rate (2 of 12)
- 83% best Objective Response (CR or PR) rate (ORR)
- 100% Clinical Benefit (CR, PR or SD) rate
- Median follow-up 6.4 months
- Patients had received a median of two prior therapies before participating in this study including chemotherapy; autologous stem cell transplant (SCT); autologous SCT and CAR-T therapy; autologous SCT and allogeneic SCT; and ibrutinib with rituximab

The combination of cirmtuzumab plus ibrutinib has been well tolerated in this study, with adverse events consistent with those reported for ibrutinib alone. There were no dose-limiting toxicities, no discontinuations and no serious adverse events attributed to cirmtuzumab alone.

"The reported complete response rate for patients with MCL treated with cirmtuzumab and ibrutinib is highly encouraging and is higher than previously reported for ibrutinib alone, particularly considering that some of these patients were heavily pre-treated. 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.

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 encouraged by the complete response rate for patients with MCL reported in the ongoing CIRLL clinical trial, and look forward to further developing cirmtuzumab in the ongoing clinical trials for patients with MCL, chronic lymphocytic leukemia (CLL) and breast cancer, as well as potentially for other ROR1-expressing solid tumors and hematological malignancies," 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 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](https://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 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](http://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 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; and statements regarding Oncternal's clinical development plans. 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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