Oncternal Therapeutics Announces Presentation of Interim Phase 1/2 Data Update for Cirmtuzumab in Combination with Ibrutinib at ASH 2020 Virtual Annual Meeting

December 7, 2020

- *Best objective response rate of 87% reported for 15 patients with relapsed/refractory mantle cell lymphoma, with a median follow-up of 12.1 months. Median progression-free survival (PFS) was not reached*
- *The combination of cirmtuzumab and ibrutinib has been well tolerated in this trial*

SAN DIEGO, Dec. 07, 2020 (GLOBE NEWSWIRE) -- 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) and chronic lymphocytic leukemia (CLL). The clinical trial is being partially funded by the California Institute for Regenerative Medicine. The data were presented at the American Society of Hematology (ASH) 2020 Virtual Annual Meeting, and a copy of the poster presentation is available online at www.oncternal.com:

- Abstract Title: Cirmtuzumab, an Anti-ROR1 Antibody, in Combination with Ibrutinib: Clinical Activity in Mantle Cell Lymphoma (MCL) or Chronic Lymphocytic Leukemia (CLL) from a Phase 1/2 Study (abstract # 2942)
- Session Title: 623. Mantle Cell, Follicular, and Other Indolent B-Cell Lymphoma – Clinical Studies: Poster III
- Session Date and Time: December 7, 2020, 7:00 a.m. - 3:30 p.m. (Pacific Time)

“The interim data from the combination of cirmtuzumab and ibrutinib are quite promising in relapsed/refractory (r/r) MCL, with an impressive 87% best ORR that has improved over time. The time to response, depth and durability of responses make cirmtuzumab a compelling candidate for further development,” 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 was also the first author on the 2020 ASCO poster presentation.

“We are pleased that median PFS has not yet been reached after a median follow-up of over 12 months in the MCL patients, and are encouraged that both PFS and ORR have improved with longer follow-up,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “We are in active dialogue with FDA on pivotal study design in order to define the path to approval in MCL.”

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

- The overall best objective response rate (ORR) was 87% (13 of 15 evaluable patients), improved over the 83% ORR reported at ASCO 2020.
- The complete response (CR) rate, determined by Cheson criteria, remains 57% (7 of 12 evaluable patients) for Part 1 of the study, and is 47% (7 of 15 evaluable patients) for Part 1 + Part 2, including the three patients from Part 2 who have shorter followup. One of the seven patients had a complete metabolic response (CMR) as assessed by PET scan, with an indeterminate bone marrow biopsy on blinded review. All complete responses remained durable, ranging from 5-25 months as of the cutoff date, with no progressions reported after achieving a CR. Six patients (40%) achieved a partial response (PR). In addition, two patients had stable disease (SD), for a total best clinical benefit rate (CR, PR and SD) of 100%.
- Median progression-free survival (PFS) was not reached, with the 95% confidence interval above 17.5 months, after a median follow-up of 12.1 months.
- Patients had received a median of two prior therapies (range 1-5) before participating in this clinical trial, with 73% of patients with two or more prior lines of therapy. Four patients had received prior treatment with ibrutinib and all four achieved clinical responses in this clinical trial, with two CRs and two PRs. Fourteen of the 15 evaluable patients (93%) had high or intermediate MCL International Prognostic Index (MIPI-b) risk score at study entry.
- Historical data published for single-agent ibrutinib for 370 patients with r/r MCL, who had received a median of two prior therapies, reported an ORR of 66%, CR rate of 20%, PR rate of 46%, and median PFS of 12.8 months (Rule et al., 2017, British Journal of Haematology).

As of the data cut-off date on October 30, 2020, 56 evaluable patients with CLL were enrolled in the dose-finding, dose-confirming and randomized cohorts of this clinical trial, 49 of whom were treated with the combination of cirmtuzumab and ibrutinib:

- Forty-five of the 49 patients achieved a clinical response, for an overall best objective response rate of 92%, including one patient who achieved a CR. In addition, four patients had stable disease, for a total clinical benefit rate (CR, PR, and SD) of 100%.

- The median PFS was not reached for patients with treatment-naïve CLL (n=19) after a median follow-up of 16.6 months, and median PFS was 29.5 months for patients with r/r CLL (n=30) after a median follow-up of 17.1 months.

The combination of cirmtuzumab plus ibrutinib has 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.

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, dose-expansion cohort in CLL and randomized Phase 2 cohort in CLL has been completed. Enrollment of the dose-expansion cohort in MCL is ongoing. 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 University of California San Diego (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. The FDA has granted Orphan Drug Designations to cirmtuzumab for the treatment of mantle cell lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma. 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 mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL) 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. The clinical pipeline also includes 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 utilizing the cirmtuzumab antibody backbone 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 including, without limitation, Oncternal’s belief that the interim results support further development of cirmtuzumab; timing and results of any discussions with the FDA regarding the MCL pivotal study design; and other statements regarding Oncternal’s 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 the risk that unforeseen adverse reactions or side effects may occur in the course of developing and testing product candidates such as cirmtuzumab, TK216 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, TK216 and its other product development programs; FDA may not agree with the study design for a pivotal trial in MCL which may increase the costs or delay the final data of such trial; the risk that the approval of one of Oncternal’s 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 its 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 finance its planned operations 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; the risk that the benefits associated with orphan drug designation may not be realized, including that orphan drug exclusivity may not effectively protect a product from competition and that such exclusivity may not be maintained; 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; the possibility that competitors may receive approval of different products for the indication for which an orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity; 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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