Oncternal Therapeutics Presents Updated Interim Data for Cirmtuzumab in Combination with Ibrutinib at ASCO 2021

May 19, 2021

- *Latest data from the CIRLL study to be presented at ASCO 2021 remain encouraging, demonstrate good, continued enrollment, are consistent with previous results and are updated over data contained in abstract #7556 released today*
- *Objective response rate (ORR) of 83% (15 of 18 evaluable patients) was observed for heavily pre-treated patients with mantle cell lymphoma (MCL) treated with cirmtuzumab plus ibrutinib compares favorably to historical ORR of 66% for ibrutinib monotherapy*
- *Complete response (CR) rate of 39% for MCL patients treated with cirmtuzumab plus ibrutinib (7 of 18 evaluable patients) compares favorably to historical ORR of 20% for ibrutinib monotherapy, with CRs remaining durable for 8-30+ months*
- *Median progression-free survival (PFS) and overall survival (OS) have not been reached for MCL patients with median follow-up of 18.9 months*
- *Median PFS and OS have also not been reached for chronic lymphocytic leukemia (CLL) patients with a median follow-up of 22.1 months*
- *The combination of cirmtuzumab and ibrutinib continues to be well tolerated, with a safety profile consistent with or slightly improved compared to historical data for ibrutinib monotherapy*

SAN DIEGO, May 19, 2021 (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, that will be presented in poster form at the American Society of Clinical Oncology (ASCO) 2021 Annual Meeting. In the CIRLL study, cirmtuzumab, an investigational anti-ROR1 monoclonal antibody, is being evaluated in combination with ibrutinib in patients with MCL and CLL. The clinical trial is being conducted in collaboration with UC San Diego School of Medicine and is partially funded by the California Institute for Regenerative Medicine.

The updated interim data will be presented at the Hematologic Malignancies—Lymphoma and Chronic Lymphocytic Leukemia session on June 7, 2021 as part of the ASCO 2021 Annual Meeting:

- **Abstract Title:** Phase 1/2 Study of Cirmtuzumab and Ibrutinib in Mantle Cell Lymphoma (MCL) or Chronic Lymphocytic Leukemia (CLL)
- **Abstract Number:** 7556
- **Session Title:** Hematologic Malignancies—Lymphoma and Chronic Lymphocytic Leukemia
- **Session Date and Time:** June 7, 2021 at 11:30 am (Eastern Time)

“These updated clinical data with the combination of cirmtuzumab and ibrutinib remain very encouraging in heavily pre-treated patients with relapsed/refractory MCL, including the impressive 83% best ORR and the durability of complete responses. The enrolled patients also had negative prognostic features, making the results even more compelling. Deep responses to cirmtuzumab plus ibrutinib after prior ibrutinib therapy are particularly intriguing. We look forward to the continuing development of cirmtuzumab,” 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 2021 ASCO poster presentation.

“We are pleased that the interim results of the CIRLL study remain strong and consistent with further follow-up, including that median PFS and OS have still not been reached for these heavily pre-treated MCL and CLL patients. Adding cirmtuzumab to ibrutinib appears well tolerated, with no apparent additional toxicities noted to date,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “We are particularly pleased with our robust enrollment to date and the number and durability of CRs for the patients with MCL. We remain in active dialogue with the US FDA concerning potential pivotal study designs and the potential pathway to seeking regulatory approval.”

The results that will be presented in poster form at ASCO 2021 include an increased population of 26 patients with relapsed/refractory MCL enrolled in the dose-finding and dose-expansion cohorts of the CIRLL clinical trial (Part 1 + Part 2), of whom 18 were evaluable for efficacy as of the April 16, 2021 data cut-off date.

- Patients had high-risk factors and were heavily pre-treated at study entry, 70% with a high Ki-67 proliferative index (≥30%), 15% with intermediate/high sMIPI prognostic score, and a median of two systemic prior therapies (range 1-5).
- The ORR of 83% (15 of 18 evaluable patients), which includes recently enrolled patients with relatively short follow-up time, is comparable to the 87% ORR (13 of 15 evaluable patients) previously presented at the American Society of Hematology (ASH) 2020 Annual Meeting.
- Eight of 18 (44%) evaluable patients achieved a partial response (PR) and two patients (11%) had stable disease (SD), for a total clinical best benefit rate (CR, PR, SD) of 94%.
- The complete response rate was 39% (7 of 18 evaluable patients). CRs have remained durable, for 8-30+ months as of

the data cutoff date.

- The clinical benefit rate and median duration of response were favorable in patients with high-risk features associated with difficult to treat disease:
    - ≥30% Ki-67: Clinical benefit rate of 89%; median duration of response of 14 months (95% CI: 8.66, NE)
    - >1 prior systemic therapy: Clinical benefit rate of 100%; median duration of response not reached
- Four patients had received prior treatment with ibrutinib and all four achieved clinical responses, with two CRs and two PRs.
- Median PFS and OS have not been reached, after a median follow-up of 18.9 months, regardless of number of prior systemic therapies, including three recently enrolled evaluable patients with a shorter follow-up time. Further, median PFS has not been reached for patients achieving a CR.
- Historical data published for single agent ibrutinib for 370 patients with relapsed/refractory MCL from three clinical trials showed an ORR of 66%, CR rate of 20% and median PFS of 12.8 months (Rule et al., 2017, British Journal of Haematology).

As of the April 16, 2021 data cut-off date, 34 patients with CLL have been enrolled in the dose-finding and dose-confirming cohorts of this clinical trial (Part 1 & Part 2), of which 34 were evaluable for efficacy. The Company plans to present updated data from the randomized cohort (Part 3) in the second half of 2021.

- Patients had high-risk factors, and most were heavily pre-treated at study entry, with 85% having RAI staging ≥2, 65% with lymphocytosis, and a median of two systemic prior therapies (range 1-15).
- The ORR is similar, 94% (32 of 34 evaluable patients), compared to a 91% ORR presented for 31 of 34 evaluable patients at ASH 2020.
- The CR rate is 15% (5 of 34 evaluable patients), 3 CRs were unconfirmed. Twenty-seven patients (79%) achieved a PR and two patients (6%) had SD, for a total clinical benefit rate (CR, PR, SD) of 100%.
- Median PFS and OS have not been reached, after a median follow up of 22.1 months, in this high risk and mostly heavily pre-treated CLL population.

The combination of cirmtuzumab plus ibrutinib has been well tolerated, with treatment emergent adverse events and hematologic abnormalities consistent with, or slightly lower than 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 MCL or CLL, 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, Oncternal is supporting two investigator-sponsored studies being conducted at the UC San Diego School of Medicine: (i) a Phase 1b clinical trial of cirmtuzumab in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer, and (ii) a Phase 2 clinical trial of cirmtuzumab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL.

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 MCL and CLL/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 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, as well as a Phase 2 clinical trial of cirmtuzumab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL. Oncternal is also developing a chimeric antigen receptor T cell (CAR-T) therapy that targets ROR1, which is currently in preclinical development as a potential treatment for hematologic cancers and solid tumors. 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 1/2 clinical trial for patients with Ewing sarcoma alone and in combination with vincristine chemotherapy. More information is available at https://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 Oncternal’s current beliefs and expectations. Forward-looking statements include statements regarding Oncternal’s belief that the interim results support further development of cirmtuzumab and Oncternal’s expectation regarding the timing and results of any discussions with the FDA, including with respect to potential pivotal study designs. Forward-looking statements are subject to risks and uncertainties inherent in Oncternal’s business, including risks associated with the clinical development and process for obtaining regulatory approval of Oncternal’s product candidates, such as potential delays in the commencement, enrollment and completion of clinical trials; the risk that results seen in a case study of one patient likely will not predict the results seen in other patients in the clinical trial; the risk that interim results of a clinical trial do not 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, as follow-up on the outcome of any particular patient continues, and as more patient data become available; and other risks described in Oncternal’s filings with the U.S. Securities and 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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