Oncternal Therapeutics Announces Opening of Randomized Phase 2 Study of Cirmtuzumab in Combination with Ibrutinib

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Interim objective response rate of 100% in evaluable patients with CLL receiving the recommended dosing regimen supports opening Phase 2

SAN DIEGO, Aug. 06, 2019 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc., (Nasdaq: ONCT) a clinical-stage biotechnology company developing potential first-in-class product candidates for cancers with critical unmet medical need, today announced that it has opened for enrollment its randomized Phase 2 study of cirmtuzumab, a ROR1-targeted monoclonal antibody, combined with ibrutinib in patients with chronic lymphocytic leukemia (CLL). The decision to open Phase 2 of the company's ongoing Phase 1/2 CIRLL (Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma) clinical trial was triggered by favorable outcomes from the Part 1 dose-finding and Part 2 dose-confirming cohorts of the clinical trial, including an observed interim objective response rate (ORR) of 100% for the first 9 CLL patients with evaluable data receiving the recommended dosing regimen who have completed 12 weeks of cirmtuzumab plus ibrutinib treatment in Part 2, and a well-tolerated safety profile consistent with that seen with ibrutinib treatment alone.

In June, the company presented data at the American Society of Clinical Oncology (ASCO) annual meeting, reporting that results from the first 12 patients with CLL treated in Part 1 of the Phase 1 portion of the study showed an observed interim objective response rate (ORR) of 91.7% for the combination of cirmtuzumab plus ibrutinib, including three patients with clinical or confirmed complete responses, and a well-tolerated safety profile consistent with that seen for ibrutinib treatment alone.

Included in the results presented at ASCO were preliminary results from six patients with mantle cell lymphoma (MCL), who were treated in a separate cohort of the CIRLL study. Data from this cohort will be presented at a future medical conference. One patient with MCL who had relapsed following an allogeneic stem cell transplant experienced a confirmed complete response (CR) after 3 months of cirmtuzumab plus ibrutinib treatment, including complete resolution of a large mediastinal mass. This CR appears to be durable, and has been confirmed after 6, 9 and 11 months of cirmtuzumab plus ibrutinib treatment.

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 at San Diego (UC San Diego).

"We are very pleased to be opening the randomized Phase 2 portion of the CIRLL study for patients with CLL and continue to be encouraged by the interim results from the study for both patients with CLL and patients with mantle cell lymphoma," said James Breitmeyer, M.D., Ph.D., Oncternal's President and CEO.

About the Study
The CIRLL Study (CIRM-0001) is a Phase 1/2 clinical trial evaluating cirmtuzumab in combination with ibrutinib in patients with CLL or MCL. Part 1 of the study was a Phase 1 dose-finding portion designed to determine the Phase 2 dose, or recommended dosing regimen (RDR). Part 2 was a Phase 1b expansion cohort to confirm the RDR. Interim analyses were specified for Part 1 and Part 2. Part 3 of the study, which is now open for enrollment, is a Phase 2 study in which approximately 90 patients with CLL will be randomized to receive either ibrutinib alone or ibrutinib plus cirmtuzumab, with a primary endpoint of complete response rate. An interim assessment of the first 12 patients with CLL enrolled in Part 1 of the study was presented as a poster at the 2019 ASCO Annual Meeting. Additional information about the CIRM-0001 study and other clinical studies 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 in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of CLL and MCL, in a collaboration with the University of California San Diego School of Medicine and the California Institute for Regenerative Medicine. 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. CIRM has also provided funding to support development programs for cirmtuzumab and a CAR-T product candidate that targets ROR1, which is currently in preclinical development as a potential treatment for hematologic cancers and solid tumors.

When expressed by hematologic malignancies such as CLL and MCL, ROR1 acts as a receptor for the tumor growth factor Wnt5a. Researchers at the UC San Diego School of Medicine discovered that targeting a critical epitope on ROR1 was key to inhibiting Wnt5a activation, specifically targeting ROR1 expressing tumors, and this finding led to the discovery of the potent and highly selective antitumor activity of cirmtuzumab observed in preclinical studies. Oncternal believes ROR1 is an attractive target for cancer therapy because it is an oncofetal antigen – a protein not normally expressed in adults, but which confers a survival and fitness advantage when reactivated and expressed by tumor cells. Preclinical data indicate that when cirmtuzumab binds to ROR1, it blocks Wnt5a signaling, induces differentiation of the tumor cells, and inhibits tumor cell proliferation, migration and survival. 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 developing a diverse pipeline of product candidates 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, a monoclonal antibody designed to inhibit the ROR1 receptor that is being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of CLL and MCL, and TK-216, a small-molecule compound that is designed to inhibit E26 transformation specific (ETS) family oncoproteins, which is being evaluated in a Phase 1 clinical trial alone and in combination

with vincristine as a treatment for Ewing sarcoma, a rare pediatric cancer. In addition, Oncternal has a CAR-T product candidate 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 belief that favorable outcomes from the ongoing Phase 1 portion of the clinical trial support opening the Phase 2 portion; and Oncternal's plans for enrolling patients in, and presenting data from, its clinical studies of cirmtuzumab. The inclusion of forward-looking statements should not be regarded as a representation by Oncternal that any of its plans will be achieved. Actual results may differ from those set forth in this release due to the risks and uncertainties inherent in Oncternal's business, including, without limitation: 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 Company's dependence on the success of cirmtuzumab and its other product development programs; 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 and Oncternal's other product candidates; the Company's limited operating history and that fact that it has incurred significant losses, and expects to continue to incur significant losses for the foreseeable future; risks related to the inability of Oncternal to obtain sufficient additional capital to continue to advance the development of cirmtuzumab and its other product candidates; 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.

Oncternal Contacts:

Investors
Richard Vincent
858-434-1113
rvincent@oncternal.com

Media
Jason Spark
619-849-6005
jason@canalecomm.com

Source: Oncternal Therapeutics