Oncternal Therapeutics Updates the Status of its Phase 1/2 Study of ONCT-808, a ROR1-Targeting Autologous CAR T, in Patients with Relapsed or Refractory Aggressive B-cell Lymphoma

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SAN DIEGO, Dec. 26, 2023 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today updated the status of its dose escalation/dose expansion Phase 1/2 Study ONCT-808-101, evaluating the company's ROR1-targeting autologous CAR T cell therapy ONCT-808 for the treatment of patients with relapsed or refractory aggressive B-cell lymphoma, including patients who have failed previous CD19 CAR T treatment.

At the initial dose of $1x10^6$ CAR T cells per kg, two of the three patients achieved complete metabolic response (CMR) and the third achieved a partial response (PR) by FDG PET-CT. Common adverse events in this dosing cohort included decreased blood counts, pneumonia and Grade 1-2 cytokine release syndrome (CRS) as of a 4 December 2023 data cutoff.

The first patient treated at the second dose level of $3x10^6$ CAR T cells per kg, an 80-year-old with bulky disease who had received four previous lines of therapy including CD19 CAR T, experienced a Grade 5 (fatal) serious adverse event consistent with CRS and immune effector cell-associated neurotoxicity syndrome (ICANS). No evidence of his lymphoma was found histologically, based on the patient's initial autopsy report.

Oncternal has been in communication and is aligned with the Food and Drug Administration (FDA) on our proposed protocol changes that include modified eligibility criteria and testing lower doses of ONCT-808 for future patients in the study.

Salim Yazji M.D., Chief Medical Officer at Oncternal Therapeutics, commented, "The safety of every patient who participates in our studies is of the utmost priority for us. We believe these early disease response data indicate that ONCT-808 is a particularly potent autologous CAR T product with the potential to address significant unmet needs for patients with aggressive B-cell malignancies. With this clear path forward, we plan to implement the protocol amendment as rapidly as possible."

About Oncternal Therapeutics
Oncternal Therapeutics is a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies for the treatment of patients with cancers that have critical unmet medical need. Oncternal pursues drug development targeting promising, yet untapped biological pathways implicated in cancer generation or progression, focusing on hematological malignancies and prostate cancer. ONCT-534 is an investigational dual-action androgen receptor inhibitor (DAARI) with preclinical activity in prostate cancer models against both unmutated androgen receptor (AR), and against multiple forms of AR aberration. It is a potential treatment for patients with mCRPC with unmet medical need because of resistance to androgen receptor inhibitors, including those with AR amplification, mutations in the AR ligand binding domain (LBD), or splice variants with loss of the AR LBD. Oncternal has initiated Study ONCT-534-101 (NCT05917470), which is open and enrolling patients for treatment with mCRPC. ONCT-808 is an investigational autologous chimeric antigen receptor T (CAR T) cell therapy that targets Receptor Tyrosine Kinase-Like Orphan Receptor 1 (ROR1) using the binding domain from zilovertamab. ONCT-808 has demonstrated activity in preclinical models against multiple hematological malignancies and solid tumors and has been shown to be specific for cancer cells expressing ROR1. Oncternal has developed a robust and reproducible manufacturing process that has the potential to reduce the time patients must wait for their individual CAR T therapy to be produced, compared with currently approved CAR T products. Oncternal has dosed patients under Study ONCT-808-101 (NCT05588440) with relapsed or refractory aggressive B-cell lymphoma, including patients who have failed previous CD19 CAR T treatment. Zilovertamab is an investigational monoclonal antibody designed to inhibit the function of ROR1. Zilovertamab has been evaluated in a Phase 1/2 Study CIRM-0001 (NCT03088878) in combination with ibrutinib for the treatment of patients with mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL) and marginal zone lymphoma (MZL), which resulted in 100% progression free survival (PFS) at 42 months in CLL patients expressing a p53 mutation/del(17p), a population underserved by current treatment options. Zilovertamab is also being evaluated in an investigator-initiated Phase 1b study of zilovertamab in combination with docetaxel in patients with metastatic castration-resistant prostate cancer (NCT05156905). More information on our company and programs 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 about the Grade 5 (fatal) serious adverse event and the ongoing work to understand the underlying cause, discussions with the FDA, potential changes to the ONCT-808-101 protocol and the potency of potential for ONCT-808 and its potential to address unmet medical needs. 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 Oncternal may not be able to resume enrollment for ONCT-808-101 in a timely manner, if at all, based on the revised protocol or otherwise, and it may be more difficult to enroll patients thereafter; the potential that any changes to the ONCT-808-101 protocol will delay the enrollment or completion of the study; 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 (including the risk that unconfirmed responses may not ultimately result in confirmed responses to treatment after follow-up evaluation), 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; later developments with the FDA may be inconsistent with the feedback received to date regarding the trial and proposed protocol; unexpected adverse side effects or inadequate efficacy of ONCT-808 that may delay or limit it development, regulatory approval and/or commercialization, or may result in clinical holds, recalls or product liability claims; 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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