Oncternal Therapeutics Announces Termination of its Clinical Studies and Exploration of Strategic Alternatives

Sep 12, 2024 at 9:00 AM EDT

SAN DIEGO, Sept. 12, 2024 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT) (the “Company”) today announced its decision to discontinue its clinical trials evaluating ONCT-534, its dual action androgen receptor inhibitor for the treatment of patients with metastatic castration resistant cancer, and ONCT-808, its ROR1-targeting autologous CAR T program for the treatment of patients with aggressive B-cell lymphoma, and to explore strategic alternatives.

In the current study, interim Phase 1 results of ONCT-534 did not show clinically meaningful improvements of disease, including prostate-specific antigen (PSA) levels, in the 20 patients treated in eight dosing cohorts with various doses and schedules of administration of ONCT-534. ONCT-534 was generally well tolerated, with dose limiting toxicity observed in 2 of 3 patients at the highest dose tested, 1200 mg given orally once per day.

The results with ONCT-808 at an interim Phase 1 analysis showed anti-tumor activity at every dose tested, including a complete metabolic response lasting eight months and long-term persistence of the CAR-T cells, with expected treatment emergent adverse events for a CAR-T therapy, and one death due to complications of shock at the highest dose tested.

Based on the available clinical data and capital requirements for continued development, the Company has decided to terminate these studies. The Company will focus on exploring strategic alternatives with the goal of maximizing value for its stockholders, which may include asset sales, licensing or other strategic transactions relating to the Company’s development programs or a merger, reverse merger, acquisition, or other business combination involving the Company. While this strategic exploration is ongoing, the Company will discontinue all product development activities and will take other steps to reduce costs, including a reduction in its workforce to preserve cash resources.

“The early results during dose escalation in the Phase 1/2 studies of ONCT-534 in heavily pretreated patients are disappointing, as the study was supported by extensive preclinical data and was designed to address important unmet medical needs for patients with advanced prostate cancer,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “In light of these data and the challenging financing environment, we intend to explore strategic options with the hope of advancing and realizing value from our pipeline including ONCT-534, ONCT-808, zilovertamab and ONCT-216.”

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. More information on our company and programs is available at https://oncternal.com/.

About ONCT-534
ONCT-534 is an investigational dual-action androgen receptor inhibitor (DAARI) with demonstrated preclinical activity in prostate cancer models against both unmutated androgen receptor (AR), and against multiple forms of AR mutation and aberration. It is a potential treatment for patients with mCRPC with unmet medical need because of resistance to androgen receptor pathway inhibitors, including those with AR amplification, mutations in the AR ligand binding domain (LBD), or splice variants with loss of the AR LBD. It is being investigated in Study ONCT-534-101 (NCT05917470) for the treatment of patients with mCRPC who are resistant to current AR pathway inhibitors.

About ONCT-808
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.

About zilovertamab
Zilovertamab (previously called cirmtuzumab and UC-961) is an investigational monoclonal antibody designed to inhibit the function of ROR1. Zilovertamab has been evaluated in 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 48 months in CLL patients whose tumors harbored p53 mutation/del(17p), a population underserved by current treatment options. The U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to zilovertamab for the treatment of CLL and MCL. The results of an investigator-sponsored, Phase 1b clinical trial of zilovertamab in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer were recently published (Shatsky 2023). Zilovertamab is being evaluated in an investigator-initiated Phase 1b study of zilovertamab in combination with docetaxel in patients with metastatic castration-resistant prostate cancer (NCT05156905), and an investigator-initiated Phase 2 clinical trial of zilovertamab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory (R/R) CLL (NCT04501939).

About ONCT-216
ONCT-216 (previously called TK216) is an investigational targeted small-molecule inhibitor of the E26 transformation-specific (ETS) family of oncoproteins including fusion proteins. Tumorigenic fusion proteins involving the EWS protein and an ETS protein can be found in most cases of

Ewing sarcoma. ETS-related translocations or overexpression are also found in many other tumors such as acute myeloid leukemia (AML), diffuse large B cell lymphoma (DLBCL), and prostate cancer. In preclinical models, ONCT-216 was observed to bind to EWS-FLI1, blocking the interaction between this fusion protein and other transcriptome proteins such as RNA helicase A, leading to tumor cell apoptosis and inhibiting tumor growth in animal models. The U.S. Food and Drug Administration (FDA) has granted Rare Pediatric Disease Designation, Orphan Drug Designation and Fast Track Status to ONCT-216 for the treatment of Ewing sarcoma. The results of a Phase 1/ 2 clinical trial of ONCT-216 in patients with Ewing sarcoma (NCT02657005) were recently published (Myers 2024).

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 ability to complete a strategic transaction or continue as a going concern even if a strategic transaction is completed; anticipated benefits of strategic transactions; and Oncternal’s ability to preserve cash during the strategic alternatives process. Forward-looking statements are subject to risks and uncertainties inherent in Oncternal’s business, including: Oncternal may not realize the benefits expected from the workforce reduction and discontinuation of product development activities, including its ability to conserve cash; Oncternal’s ability to retain remaining key personnel; whether Oncternal will be able to secure and complete or achieve the anticipated benefits from any potential strategic transactions on acceptable terms or at all; Oncternal may use its capital resources sooner than it anticipates, resulting in a liquidation and dissolution of the Company; Oncternal’s common stock may be delisted from Nasdaq; 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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