Oncternal Therapeutics Announces Updated Safety and Efficacy Data for Phase 1/2 Study of ONCT-534 for the Treatment of R/R Metastatic Castration-Resistant Prostate Cancer

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SAN DIEGO, Oct. 22, 2024 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT) (the "Company") today announced updated data from its Phase 1/2 Study of ONCT-534 for the treatment of patients with relapsed or refractory metastatic Castration-Resistant Prostate Cancer (mCRPC).

Based on initial pharmacokinetic results, two additional dosing cohorts with twice daily (BID) oral dosing of ONCT-534 had been incorporated in the Phase 1/2 study ONCT-534-101 (NCT05917470). Overall, fifteen patients received ONCT-534 once daily (QD) in six dosing cohorts and six patients received ONCT-534 BID in two dosing cohorts. Based on a data cut off of September 30, 2024, the BID dosing schedule was well tolerated, with no related Grade 3 or higher toxicities. One patient, who experienced a rising PSA on ONCT-534 at 160 mg BID, had a subsequent 50% reduction in PSA after four weeks of ONCT-534 at 300 mg BID, and at the same time the CAT Scan showed a 16% reduction in target lesions compared to baseline. Enumeration and biomarker analysis of circulating tumor cells (CTCs) showed promising effects on expression of androgen receptor (AR)-regulated genes, and AR nuclear translocation in six additional patients. CTC analysis also showed that some patients who did not respond to ONCT-534 had prostate cancer that had developed neuroendocrine features, which are associated with AR independent disease.

"While we still believe the decision to discontinue the ONCT-534-101 clinical trial remains the correct one in the current biotechnology environment, the updated clinical results highlight the potential of ONCT-534 in prostate cancer. We believe there is value in exploring BID dosing further, as well as studying ONCT-534 in earlier lines of therapy for advanced prostate cancer," said James Breitmeyer, M.D., Ph.D., Oncternal's President and CEO. "We continue to explore strategic alternatives for our product candidates, including ONCT-534, ONCT-808, zilovertamab and ONCT-216 in an ongoing effort to maximize value to our shareholders."

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 was 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. It was investigated in 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 Receptor Tyrosine Kinase-Like Orphan Receptor 1 (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 del(17p)/p53 mutation, 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 was 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; Oncternal’s ability to preserve cash during the strategic alternatives process; and the potential of ONCT-534. 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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