Oncternal Therapeutics Presents Updated Interim Data for TK216 in Patients with Relapsed or Refractory Ewing Sarcoma in an Oral Session at ASCO 2021

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- *Latest data from study TK216-01 remain encouraging, are consistent with previous results, and are updated over data contained in ASCO Abstract #11500 released today*
- *Two patients who achieved a complete response (CR) remain with no evidence of disease, one for over 24 months and the other for over 14 months on study*
- *TK216 remained generally well tolerated with a manageable safety profile*

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 oral presentation on its ongoing Phase 1/2 clinical trial evaluating TK216, an investigational, potentially first-in-class, targeted small-molecule inhibitor of the E26 transformation-specific (ETS) family of oncoproteins, in patients with relapsed or refractory Ewing sarcoma, to be presented at the American Society of Clinical Oncology (ASCO) 2021 Annual Meeting.

Ravin Ratan, M.D., Assistant Professor, Department of Sarcoma Medical Oncology, Division of Cancer Medicine, University of Texas MD Anderson Cancer Center, will present at the ASCO 2021 Annual Meeting Sarcoma oral session that two heavily pre-treated and metastatic Ewing sarcoma patients treated at the recommended Phase 2 dose (RP2D) of TK216 continue to demonstrate prolonged complete regression of Ewing sarcoma for greater than one and two-years on study and have tolerated ongoing treatments well with TK216 alone or in combination with vincristine.

The data will be presented at the ASCO 2021 Annual Meeting:

- **Abstract Title**: TK216 for Relapsed/Refractory Ewing Sarcoma: Interim Phase 1/2 Results
- **Abstract number:** 11500
- **Session Title:** Sarcoma
- **Session Date and Time:** June 4, 2021, from 1:30 – 4:30 p.m. (Eastern Time)

“I am optimistic about the durable disease control observed in the two heavily pre-treated metastatic patients with Ewing sarcoma, and that both tolerated their treatments with TK216 with or without vincristine well,” said Dr. Joseph Ludwig, M.D. Department of Sarcoma Medical Oncology, Division of Cancer Medicine, University of Texas MD Anderson Cancer Center. “Advanced, refractory Ewing sarcoma is a serious and devastating condition, and novel therapies are desperately needed. These encouraging interim results from study TK216-01, along with evolving preclinical data, suggest that this agent may warrant further clinical development.”

As of the April 16, 2021 data cut-off date, a total of 68 patients with relapsed/refractory Ewing sarcoma have been treated with TK216 in study TK216-01, 29 patients in the dose-finding cohorts, and 39 patients treated at the RP2D of TK216 (200 mg/m^2/day for 14 days) with vincristine 0.75-1.5 mg/m^2 administered on the first day of each cycle. All patients treated at the RP2D had metastases at study entry and were heavily pretreated, with a median number of three prior systemic therapies (range 1-8). Two patients treated at the RP2D have achieved marked and sustained regression in target lesions after as little as two cycles of therapy. The first patient experienced 100% regression of target lesions following two cycles of TK216 alone. After six cycles of treatment that included concomitant vincristine starting in the third cycle, a single 7 mm non-target lung lesion was resected, resulting in a surgical complete remission. The patient remained on study with no evidence of disease after more than 24 months. The second patient attained 90% resolution of target lung lesions following two cycles of TK216 plus vincristine, then achieved a CR after six cycles of therapy. This patient also remained on study disease-free after more than 14 months, treated with TK216 alone following cycle 5. At the RP2D, the objective response rate (ORR) was 9.7% (3 of 31 evaluable patients), including one patient with an unconfirmed partial response (PR). Eleven patients (35.5%) had stable disease (SD), for a disease control rate (CR, PR, SD) of 45.2% (14 of 31 evaluable patients). The median progression-free survival (PFS) for patients treated at the RP2D was 1.9 months (95% CI: 1.5, 3.0), with an encouraging tail of extended PFS for some patients. Updated safety data showed that TK216 at the RP2D has been generally well tolerated, with frequent side effects including myelosuppression, fatigue, and alopecia. No unexpected off-target toxicities or deaths related to TK216 toxicity have been observed.

“We are encouraged by the durable clinical responses in this updated clinical data set, and the sustained disease control observed in two heavily pre-treated patients with refractory metastatic Ewing sarcoma treated with TK216 with or without vincristine,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “This first-in-class investigational agent may also have potential in a variety of other malignancies driven by ETS alterations including acute myeloid leukemia, large B-cell lymphoma and prostate cancer.”

About TK216
TK216 is an investigational, potentially first-in-class, 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 prostate cancer, acute myeloid leukemia (AML) and diffuse large B-cell lymphoma (DLBCL). TK216 was developed based on discoveries in the laboratory of Jeffrey Toretsky, M.D., at Georgetown Lombardi Comprehensive Cancer Center, who discovered inhibitors of EWS-FLI1 using a novel chemical screening assay. In preclinical models, TK216 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 Orphan Designation,

Fast Track designation, and Pediatric Rare Disease Designation to TK216 for the treatment of Ewing sarcoma. TK216 is an investigational medication that has not been approved by the FDA for any indication.

About Study TK216-01
TK216 is being evaluated in an ongoing Phase 1/2 clinical study as a single agent and in combination with vincristine in patients with relapsed or refractory Ewing sarcoma, a rare pediatric cancer with no standard treatment available after first-line chemotherapy. The dose-finding portion of the study is complete. Oncternal is currently enrolling patients in a Phase 2 expansion cohort to evaluate the clinical response of treatment with TK216 in combination with vincristine using the recommended Phase 2 dosing regimen. This multi-center study is enrolling patients at nine clinical trial centers across the U.S. Additional information about the TK216 study may be accessed at ClinicalTrials.gov (NCT02657005).

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 an 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 beliefs that further clinical testing of TK216 is warranted and that TK216 has potential to treat other indications. 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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