Oncternal Therapeutics Announces Presentation of Interim Clinical Data on TK216, its First-in-class, Targeted ETS Inhibitor, in Patients with Relapsed or Refractory Ewing Sarcoma at the CTOS 2019 Annual Meeting

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- *Interim data from Phase 1 study in patients with Ewing sarcoma show TK216 has been generally well tolerated*
- *One of two patients at the current, highest TK216 exposure dose regimen has experienced a deep and sustained clinical response*
- *Dose-finding and schedule escalation cohorts of the Phase 1 study nearing completion*
- *TK216 has been granted Orphan Designation and Fast Track designation for the treatment of relapsed/refractory Ewing sarcoma*

SAN DIEGO--(BUSINESS WIRE)--Nov. 14, 2019-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced the presentation of interim clinical data from its ongoing Phase 1 clinical trial evaluating TK216, a first-in-class, targeted, investigational small-molecule inhibitor of the E26 transformation-specific (ETS) family of oncoproteins, in patients with relapsed or refractory Ewing sarcoma. Paul A. Meyers, M.D., Chief, Pediatric Sarcoma Service and Vice Chair for Clinical Affairs of Memorial Sloan Kettering Cancer Center, reported at the Connective Tissue Oncology Society (CTOS) 2019 Annual Meeting in Tokyo, Japan that one of two patients treated in the current, highest exposure dose cohort of Study TK216-01 is without evidence of Ewing sarcoma after eight months on study, and has tolerated treatments with TK216 alone or combined with vincristine well.

“We are encouraged by this first reported deep and sustained clinical response to TK216 in a patient with Ewing sarcoma in the dose-finding portion of our clinical trial and look forward to further evaluating the recommended Phase 2 dose regimen of TK216 in a larger number of patients with this devastating disease,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “This first-in-class investigational agent may also be applicable in other malignancies driven by ETS alterations including AML and prostate cancer, which we continue to explore in preclinical studies.”

Study TK216-01, Oncternal’s ongoing Phase 1 study of TK216 in patients with relapsed or refractory Ewing sarcoma, is a first-in-human, multicenter clinical trial. Trial objectives include the evaluation of safety, tolerability, pharmacokinetics and tumor response. Thirty-two patients have been treated in the dose-finding part of the trial. Patients entering the trial had previously been treated with a median of four, and up to nine prior lines of systemic therapy. TK216 has been generally well tolerated in this trial, with common side effects including myelosuppression, fatigue, nausea and alopecia. The maximum tolerated dose has been identified as 220 mg/m^2/day for a seven-day treatment regimen, and 200 mg/m^2/day for a 10-day regimen. Dose limiting toxicities consisted of transient and manageable myelosuppression, primarily neutropenia. No unexpected off-target toxicities have been observed.

One of two patients treated at the current, highest exposure dose regimen (200 mg/m^2/day for 14 days) has experienced a deep and sustained clinical response to TK216. Multiple lung nodules regressed following two cycles of TK216 alone. After six months of treatment that included concomitant vincristine starting in the third cycle, a single 7 mm lung nodule was resected, resulting in a surgical complete remission. The patient remains with no evidence of disease after eight months of treatment. TK216, with or without vincristine, has been well tolerated by this patient, with only minimal myelosuppression. Clinical pharmacology data suggest that this dosing regimen may result in drug levels that meet or exceed those that killed tumor cells *in vitro* and inhibited tumor growth in animal models.

Enrollment of the final dose-finding cohort of the study is nearing completion, after which Oncternal intends to begin enrolling patients using the recommended Phase 2 dosing regimen in an expansion cohort to further evaluate the clinical response to treatment.

“I am encouraged by the depth and duration of response to TK216 in this heavily pre-treated patient with Ewing sarcoma, and that the patient tolerated his treatments with TK216 and vincristine well,” said Dr. Meyers. “Advanced, refractory Ewing sarcoma is a serious and devastating condition, and novel therapies are desperately needed. These interim results of Study TK216-01, along with evolving preclinical data, suggest that this agent warrants further clinical testing in Ewing sarcoma as well as in other cancer indications.”

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 and acute myeloid leukemia (AML). 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 and Fast Track 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 the Study

TK216 is being evaluated in a Phase 1 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 nearing

completion, after which Oncternal intends to begin enrolling patients in an 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 actively enrolling patients at seven 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 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 chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL), and TK216, an investigational targeted small-molecule inhibitor of the ETS family of oncoproteins, that is being evaluated in a Phase 1 clinical trial for patients with Ewing sarcoma alone and in combination with vincristine chemotherapy. In addition, Oncternal has a program to develop a CAR-T therapy 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 beliefs, goals, intentions and expectations, and include: the company’s expectation that the dose-finding and schedule escalation cohorts of its ongoing Phase 1 clinical trial of TK216 is nearing completion; that Oncternal intends commencing enrollment in a Phase 2 clinical study in a larger number of patients; the company’s belief that the interim results of the ongoing Phase 1 clinical trial of TK216 and preclinical data suggest that further clinical testing of TK216 in other cancer indications, including malignancies driven by ETS alterations, is warranted. Forward-looking statements are subject to risks and uncertainties inherent in Oncternal’s business, which include, but are not limited to: 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 and treatment 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 TK216 and Oncternal’s other product candidates, which could adversely impact the company’s ability to complete clinical trials and obtain regulatory approval for such product candidates; uncertainties associated with the clinical development and process for obtaining regulatory approval of TK216 and Oncternal’s other product candidates, including potential delays in the commencement, enrollment and completion of clinical trials; the risk that fast track designation may not actually lead to a faster development or regulatory review or approval process for TK216, and that obtaining orphan drug exclusivity for TK216 may not effectively protect the product from competition; Oncternal’s dependence on the success of TK216 and its other product development programs; the risk that the regulatory landscape that applies to the development program for TK216 and the company’s other product candidates may change, which could result in delays or termination of development of such product candidates or unexpected costs in obtaining regulatory approvals; Oncternal’s limited operating history and the fact that it has incurred significant losses, and expects to continue to incur significant losses for the foreseeable future; the risk that the company may not be able to obtain sufficient additional financing when needed or at all as required to achieve its goals, which could force the company to delay, limit, reduce or terminate its product development programs or other operations, 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.

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