



Oncternal Therapeutics Announces Opening of Phase 1b Expansion Cohort of Clinical Trial of TK216, Targeted ETS Inhibitor, in Patients with Ewing Sarcoma

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- *Dose-finding cohort demonstrated clinical activity and was generally well-tolerated*
- *TK216 has been granted Orphan Drug and Fast Track Designations for treatment of patients with relapsed/refractory Ewing sarcoma*

SAN DIEGO--(BUSINESS WIRE)--Dec. 11, 2019-- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced that it has opened for enrollment a Phase 1b expansion cohort of its ongoing 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.

The decision to open an expansion cohort was based on favorable interim results from the dose-finding cohort of the trial, including a deep and sustained clinical response reported for one of the patients treated at the current, highest exposure dose regimen, who is without evidence of Ewing sarcoma after more than eight months on study and has tolerated treatments with TK216, alone and in combination with vincristine, well. TK216 has been generally well tolerated in this trial. Dose limiting toxicities consisted of transient and manageable myelosuppression, primarily neutropenia.

The expansion cohort will further evaluate the recommended Phase 2 dose regimen of TK216 (200 mg/m²/day for 14 days) in combination with vincristine and is anticipated to enroll approximately 18 patients with relapsed or refractory Ewing sarcoma.

"We are encouraged by the initial clinical activity demonstrated by TK216 in the dose-finding portion of this clinical trial in patients with relapsed/refractory Ewing sarcoma 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 targeted investigational agent may also be applicable in other malignancies driven by ETS alterations including acute myeloid leukemia (AML) and prostate cancer, which we continue to explore in preclinical studies."

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 has been completed, and Oncternal is actively 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](https://clinicaltrials.gov/ct2/show/study/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 plans to enroll patients in the expansion cohort of the ongoing clinical study of TK216, and its belief that TK216 may also be applicable in other cancer indications. 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, including interim response results, which may not be confirmed by later assessments, 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 by the FDA may not actually lead to a faster development or regulatory review or approval process for TK216, and that having orphan drug exclusivity for TK216 may not provide benefits associated with orphan drug designation, including the potential for market exclusivity; 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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