Oncternal Therapeutics Announces Presentation of Interim Phase 1 Clinical Trial Data for TK216 in Patients with Relapsed/Refractory Ewing Sarcoma at ESMO Virtual Congress 2020

September 21, 2020

- Complete responses reported for two patients with relapsed/refractory Ewing sarcoma treated at the recommended Phase 2 dose of TK216, including a patient who recently improved from a partial to complete response

- Enrollment in expansion cohort has accelerated, and data on additional patients are planned for presentation in the fourth quarter of 2020

SAN DIEGO--(BUSINESS WIRE)--Sep. 21, 2020-- 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, 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. Joseph A Ludwig, M.D., Associate Professor in the Department of Sarcoma Medical Oncology at The University of Texas MD Anderson Cancer Center, presented the results in an oral presentation at the European Society for Medical Oncology (ESMO) Virtual Congress 2020 on September 20, 2020.

“I am very encouraged by the complete responses to TK216 in these two heavily pre-treated patients with Ewing sarcoma,” said Dr. Ludwig. “Advanced, refractory Ewing sarcoma is a serious and devastating condition, with no approved therapies, and novel therapeutic approaches are desperately needed. These positive interim clinical results suggest that TK216 holds promise for patients with Ewing sarcoma with no alternatives and poor prognoses.”

This ongoing clinical trial is a first-in-human, multicenter Phase 1 study of TK216 in patients with relapsed or refractory Ewing sarcoma. Trial objectives include the evaluation of safety, tolerability, pharmacokinetics, and tumor response. Patients entering the trial had previously been treated with a median of three, and as many as eleven prior lines of systemic therapy. TK216 has been generally well tolerated in this trial, with common side effects including myelosuppression, fatigue, nausea and alopecia. Dose limiting toxicities consisted of transient and manageable myelosuppression, primarily neutropenia. No unexpected off-target toxicities have been observed. The recommended Phase 2 dose (RP2D) has been established to be 200 mg/m^2/day of TK216 for 14 days in combination with vincristine chemotherapy dosed at 0.75 mg/m^2 on the first day of each treatment cycle.

Key Updates: The presentation included interim data for 15 evaluable patients treated at the RP2D as of the August 13, 2020 cut-off date. Two of the 15 patients have now achieved complete responses (CR), including one surgical CR. One of these patients was previously categorized as a partial responder after two treatment cycles and converted to a complete response after his 6th cycle. Five patients had stable disease (SD), for a disease control rate (CR, partial response or SD) of 47%.

The first patient achieving a CR initially presented with metastatic Ewing sarcoma involving the clavicle and lungs and had received four prior lines of systemic therapy as well as surgery and radiation and was progressing when he enrolled in this clinical trial. The patient experienced a deep and sustained partial clinical response following two cycles of TK216 alone, with resolution of all target lung metastases. 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 on treatment, with no evidence of disease, at about 1.5 years in this clinical trial.

The second patient achieving a CR initially presented with metastatic Ewing sarcoma involving the kidney area and lungs. He relapsed following initial chemotherapy, radiation, and surgery before enrolling in this clinical trial. The patient achieved a partial response with a 90% reduction of all lesions following two cycles of therapy and achieved a complete response after six cycles. The patient remains on treatment, with no evidence of disease at about seven months in this clinical trial.

Pharmacokinetic data from the clinical trial showed that TK216 drug levels at the RP2D exceeded plasma levels associated with anti-tumor activity in preclinical models.

“We are excited by the deepening clinical responses over time, with now two complete responses reported for patients with Ewing sarcoma treated with TK216,” said James Breitmeyer, M.D., Ph.D., President and CEO, Oncternal. “Enrollment in the expansion cohort of this clinical trial has accelerated despite the COVID-19 pandemic, and we plan to present additional data from over 16 patients with relapsed/refractory Ewing sarcoma treated at the RP2D at a scientific conference in the fourth quarter of 2020.”

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 complete, and patients are now being enrolled in the expansion cohort. This multi-center study is actively 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, 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 including, without limitation, whether the interim results suggest that TK216 holds promise for patients with Ewing sarcoma; the numbers of patients expected to be enrolled and anticipated dates for announcing results from the ongoing Phase 1 clinical trial in patients with relapsed/refractory Ewing sarcoma; and other statements regarding Oncternal’s development plans. 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 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 cirmtuzumab, 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; Oncternal has encountered delays, and may encounter additional delays or difficulties, in enrolling patients in its clinical trials as a result of the COVID-19 pandemic; the COVID-19 pandemic may disrupt Oncternal’s business operations, increasing its costs; uncertainties associated with the clinical development and process for obtaining regulatory approval of cirmtuzumab and Oncternal’s other product candidates, including potential delays in the commencement, enrollment and completion of clinical trials; Oncternal’s dependence on the success of cirmtuzumab and its other product development programs; the risk that the regulatory landscape that applies to the development program for cirmtuzumab, TK216 and the company’s other product candidates may change over time; the risk that the approval of one of Oncternal’s product candidates may be blocked for seven years if a competitor obtains approval of the same drug or biologic, as defined by the FDA, or if its product candidate is determined to be contained within the competitor’s product for the same indication or disease; the risk that competitors may develop technologies or product candidates more rapidly than Oncternal, or that are more effective than Oncternal’s product candidates, which could significantly jeopardize Oncternal’s ability to develop and successfully commercialize its product candidates; 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 will have insufficient funds to finance its planned operations and 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; the risk that the benefits associated with orphan drug designation may not be realized, including that orphan drug exclusivity may not effectively protect a product from competition and that such exclusivity may not be maintained; the risk that, if an orphan designated product, including cirmtuzumab, receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity; the possibility that competitors may receive approval of different products for the indication for which an orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity; 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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