Oncternal Therapeutics Deprioritizes Development of ONCT-216 to Focus Resources on Phase 3 Trial for Zilovertamab in the Treatment of Mantle Cell Lymphoma

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- *Discontinued enrollment of Phase 1/2 trial of ONCT-216 in Ewing sarcoma*
- *Resources will be primarily reallocated to our zilovertamab global registrational Phase 3 study ZILO-301, which is expected to be initiated in Q3 2022*
- *Focus on advancing preclinical assets for hematological malignancies and prostate cancer, including expected submission of IND for our ROR1-targeting CAR-T cell therapy candidate, ONCT-808, in mid-2022 and execution of IND-enabling studies for our novel dual-action androgen receptor inhibitor (DAARI) program, ONCT-534*
- *Cash runway to fund operations guidance extended well into Q3 2023; with an estimated $82.2 million in cash and cash equivalents and no debt as of March 31, 2022*

SAN DIEGO, April 13, 2022 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced that it has deprioritized further development of ONCT-216 to reallocate resources to zilovertamab, the Company's investigational anti-ROR1 monoclonal antibody, and its Phase 3 registrational trial that the Company expects to initiate in Q3 2022. As such, the Company has discontinued enrollment in the Phase 1/2 study evaluating ONCT-216 in patients with relapsed or refractory Ewing sarcoma.

"This asset prioritization allows us to further sharpen our focus on hematological malignancies and prostate cancer, while deploying our capital towards meaningful catalysts as we navigate this historically challenging pandemic, geopolitical and capital markets macroenvironment," said James Breitmeyer, MD, PhD, Oncternal's President and CEO. "We believe this focused approach, along with prudent cash management, will enable us to fund our operations well into the third quarter of 2023, as we continue to explore all potential sources of capital to enable us to reach our milestones."

The Company expects to initiate its global registrational Phase 3 Study ZILO-301 in the third quarter of 2022, taking into account the impact of geopolitical factors and COVID-19 related supply chain issues. The study will randomize patients with relapsed or refractory MCL who have experienced stable disease or a partial response after receiving four months of oral ibrutinib therapy to receive either blinded zilovertamab or placebo, and all patients will continue receiving oral ibrutinib. The novel ZILO-301 design is supported by encouraging data from the Company's ongoing Phase 1/2 clinical trial of zilovertamab plus ibrutinib for patients with MCL or CLL, as well as by a successful End-of-Phase-2 meeting with the U.S. Food and Drug Administration (FDA).

The Company's lead autologous ROR1-targeted CAR-T cell therapy program candidate, ONCT-808, is advancing according to plan towards an Investigational New Drug (IND) application submission expected in mid-2022, based on supportive manufacturing and preclinical data as well as a productive pre-IND meeting with the FDA earlier this year.

Finally, the Company continues to advance ONCT-534, its lead candidate in its DAARI program, and expects to initiate IND-enabling GLP toxicology studies and GMP manufacturing later this quarter. ONCT-534 has shown anti-tumor activity in preclinical studies relevant to multiple clinically important forms of resistance for patients with prostate cancer, including those involving overexpression of the androgen receptor, or expression of mutants of the androgen receptor, or splice variants such as AR-V7.

About Zilovertamab (formerly Cirmtuzumab)
Zilovertamab is an investigational, humanized, potentially first-in-class monoclonal antibody targeting Receptor tyrosine kinase-like Orphan Receptor 1 (ROR1). Zilovertamab is currently being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of patients with MCL or chronic lymphocytic leukemia (CLL), in a collaboration with the University of California San Diego (UC San Diego) School of Medicine and the California Institute for Regenerative Medicine (CIRM). In addition, Oncternal is supporting two investigator-sponsored studies being conducted at the UC San Diego School of Medicine, a Phase 1b clinical trial for patients with metastatic castration-resistant prostate cancer (mCRPC), and a Phase 2 clinical trial of zilovertamab in combination with venetoclax, a Bcl-2 inhibitor, for patients with relapsed/refractory CLL. Both are open for enrollment.

ROR1 is a potentially attractive target for cancer therapy because it is an onco-embryonic antigen, not usually expressed on adult cells, but its expression confers a survival and fitness advantage when reactivated and expressed by tumor cells. Researchers at the UC San Diego School of Medicine discovered that targeting a critical epitope on ROR1 was key to specifically inhibiting ROR1 expressing tumors. This led to the development of zilovertamab which binds this critical epitope of ROR1, highly expressed on many different cancers but not on normal tissues. Preclinical data showed that when zilovertamab bound to ROR1, it blocked Wnt5a signaling, inhibited tumor cell proliferation, migration and survival, and induced differentiation of the tumor cells. The FDA has granted Orphan Drug Designations to zilovertamab for the treatment of patients with MCL and CLL/small lymphocytic lymphoma. Zilovertamab is in clinical development and has not been approved by the FDA for any indication.

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. The clinical pipeline includes zilovertamab, an investigational monoclonal antibody designed to inhibit ROR1, a type I tyrosine kinase-like orphan receptor. Zilovertamab 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), in investigator-initiated studies, including a Phase 1b clinical trial in combination with paclitaxel for the treatment of

women with HER2-negative metastatic or locally advanced, unresectable breast cancer, in a Phase 2 clinical trial of zilovertamab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL, and in a Phase 1b study of zilovertamab in combination with docetaxel in patients with metastatic castration-resistant prostate cancer (mCRPC). Oncternal is also developing ONCT-808, 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 early-stage pipeline also includes ONCT-534 , a dual-action androgen receptor inhibitor (DAARI), that is in preclinical development as a potential treatment for castration resistant prostate cancer and other androgen-receptor dependent diseases. 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 development programs, including Oncternal’s estimated cash and cash equivalents as of March 31, 2022, the anticipated timing for announcing additional preclinical and clinical data; timing of reaching any milestones, including IND submissions; timing for regulatory communications; Oncternal’s expected cash runway; and the potential that Study ZILO-301 can serve as a registrational clinical trial; and the expected initiation of clinical trials, including Study ZILO-301. 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; we have not conducted head-to-head studies of zilovertamab in combination with ibrutinib compared to ibrutinib monotherapy and data from separate studies may not be directly comparable due to the differences in study protocols, conditions and patient populations; 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; later developments with the FDA may be inconsistent with the minutes from the completed end of Phase 2 meeting, including that the proposed Study ZILO-301 that may not support registration of zilovertamab in combination with ibrutinib which is a review issue with the FDA upon submission of a BLA; 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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