Oncternal Therapeutics Announces Clinical Trial Collaboration to Advance Zilovertamab Phase 3 Study in combination with Ibrutinib for Patients with MCL

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- *Clinical trial collaboration supports global registrational Phase 3 study ZILO-301, to treat patients with relapsed or refractory MCL with zilovertamab plus ibrutinib*
- *Agreement is supportive of the planned initiation of ZILO-301 in Q3 2022 and will also supply ibrutinib for the open-label companion study ZILO-302*

SAN DIEGO, July 14, 2022 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced it entered into a clinical trial collaboration with Pharmacyclics, an AbbVie company, that includes supply of ibrutinib for its Phase 3 clinical trial.

“This agreement represents a significant milestone for Oncternal as we advance towards the planned initiation of our registrational study ZILO-301 in the third quarter of 2022,” said James Breitmeyer, M.D., Ph.D., Oncternal’s President and CEO. “Ibrutinib was the first Bruton’s tyrosine kinase (BTK) inhibitor in the market and its approval changed the treatment paradigm for patients suffering from certain hematological malignancies. We are pleased that this collaboration will support the development of an innovative combination of zilovertamab and ibrutinib that we believe may address important unmet needs of patients with MCL.”

Under the terms of the collaboration, the supply of ibrutinib will support the company’s global registrational Phase 3 clinical trial of zilovertamab for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL), ZILO-301. The agreement also includes the supply of ibrutinib for Study ZILO-302, an open-label companion study of zilovertamab plus ibrutinib for patients who have progressive disease during the initial four months of ibrutinib monotherapy from Study ZILO-301.

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, chronic lymphocytic leukemia (CLL) or marginal zone lymphoma (MZL), 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 cancers, including those with clinically important resistance to approved androgen receptor inhibitors. 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 the potential that Study ZILO-301 can serve as a registrational clinical trial; and the expected initiation and enrollment 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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