Oncternal Therapeutics Announces Agreement with U.S. FDA on Phase 3 Registrational Study Design for Zilovertamab in the Treatment of Mantle Cell Lymphoma

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- *The company reached consensus with the FDA on the design and major details of the Phase 3 superiority Study ZILO-301, to treat patients with relapsed or refractory MCL with zilovertamab plus ibrutinib*
- *The FDA also provided positive feedback on the proposed key clinical and regulatory requirements of Oncternal's development program for zilovertamab in MCL*
- *Global registrational Study ZILO-301 is expected to be initiated in the second quarter of 2022*
- *Oncternal Therapeutics will host a conference call today at 4:30 p.m. ET to provide further details*

SAN DIEGO, Jan. 04, 2022 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced that following a successful End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) for zilovertamab, the company's investigational anti-ROR1 monoclonal antibody, the company and the FDA agreed on key elements of the company's potentially pivotal Phase 3 clinical trial of zilovertamab for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL). The FDA has also reviewed and agreed upon the key design features and operational details of the company's Phase 3 clinical trial protocol and Statistical Analysis Plan, which is being finalized based on the FDA's input.

"The completion of End-of-Phase 2 meetings and consensus on clinical trial design and other program elements mark a meaningful and encouraging milestone for Oncternal Therapeutics," said James Breitmeyer, MD, PhD, Oncternal's President and CEO. "The agreement underscores our productive dialogue with the FDA on key elements of our program and the Phase 3 clinical trial design as we align on the potential path to commercialization for zilovertamab, which offers potential advantages to patients suffering from aggressive lymphomas such as MCL. The positive data from our ongoing Phase 1/2 CIRLL study recently presented at ASH 2021 underscore those advantages and are supportive of our registration strategy."

The Phase 3 superiority clinical trial ZILO-301 is entitled, "Randomized, Double-blind, Placebo-controlled, Multi-center Phase 3 Study of Zilovertamab (A ROR1 Antibody) Plus Ibrutinib Versus Ibrutinib Plus Placebo in Patients with Relapsed or Refractory Mantle Cell Lymphoma." Michael Wang MD, Endowed Professor in the Department of Lymphoma & Myeloma at MD Anderson Cancer Center, will serve as the U.S. Principal Investigator and Chairman of the steering committee for this study. 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 primary endpoint, intended to support submission of a Biologics License Application (BLA) seeking regular FDA approval, will be progression-free survival (PFS). An interim analysis potentially supporting submission of a BLA seeking accelerated FDA approval will be conducted with a primary endpoint of Overall Response Rate (ORR) plus Duration of Response (DOR). The FDA previously provided positive feedback on the sufficiency of the preclinical and pharmacology studies of zilovertamab needed to support a BLA submission.

Study ZILO-301 will be conducted internationally in at least 50 centers with demonstrated expertise treating MCL, with initiation expected in the second quarter of 2022. Sample size calculations are being finalized for this novel enrichment study, based on input from the FDA.

The company is also planning to conduct 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.

Oncternal Therapeutics will host a conference call today at 4:30 p.m. ET to provide further details on this important milestone. The live webcast of the call will be available online at investor.oncternal.com and the call will be archived there for at least 30 days.

The company will also provide details on its overall pipeline advancement during an R&D Day on January 25, 2022.

About Zilovertamab (formerly Cirmtuzumab)
Zilovertamab is an investigational, potentially first-in-class monoclonal antibody targeting ROR1, or Receptor tyrosine kinase-like Orphan Receptor 1. Zilovertamab is currently being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of 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: (i) a Phase 1b clinical trial of zilovertamab in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer, and (ii) a Phase 2 clinical trial of zilovertamab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL.

ROR1 is a potentially attractive target for cancer therapy because it is an onco-embryonic antigen – not usually expressed on adult cells, and 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 targeting ROR1 expressing tumors. This led to the development of zilovertamab, that binds this critical epitope of ROR1, which is 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 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 zilovertamab (formerly 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 1b/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, as well as a Phase 2 clinical trial of zilovertamab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL. 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 clinical pipeline also includes ONCT-216 (formerly TK216), an investigational targeted small-molecule inhibitor of the ETS family of oncoproteins, that is being evaluated in a Phase 1/2 clinical trial for patients with Ewing sarcoma alone and in combination with vincristine chemotherapy. The early-stage pipeline also includes ONCT-534 (formerly GTX-534), a dual-action androgen receptor inhibitor, that is in pre-clinical 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 the potential for zilovertamab in combination with ibrutinib to treat MCL or CLL; the potential that ZILO-301 can serve as a registrational clinical trial; and the expected initiation of, and elements constituting, the ZILO-301 and ZILO-302 studies. 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 ZILO-301 trial 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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