Oncternal Therapeutics Presents Rationale and Plans for its Registrational Phase 3 Study Evaluating Zilovertamab in Combination with Ibrutinib at the EHA 2022 Congress

June 10, 2022

SAN DIEGO, June 10, 2022 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced that the rationale and plans for its upcoming Phase 3 ZILO-301 (zilovertamab plus ibrutinib targeting ROR1 for patients with Mantle Cell Lymphoma) clinical trial will be highlighted in a poster presentation at the European Hematology Association (EHA) 2022 Hybrid Congress. ZILO-301 is designed to evaluate the efficacy and safety of zilovertamab, an investigational anti-ROR1 monoclonal antibody, plus ibrutinib compared to ibrutinib monotherapy for the treatment of patients with relapsed or refractory mantle cell lymphoma (R/R MCL).

- **Poster Title:** Study ZILO-301: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Zilovertamab Plus Ibrutinib vs. Ibrutinib in Patients with Relapsed or Refractory Mantle Cell Lymphoma
- **Abstract Number:** P1154
- **Session Title:** Indolent and mantle-cell non-Hodgkin lymphoma - Clinical
- **Session Date and Time:** June 10, 2022 at 16:30 CEST

“The recently announced updated interim data from our Phase 1/2 study presented at ASCO 2022, provides ample support for the rationale of the design of our global registration Phase 3 study, ZILO-301, evaluating the combination of zilovertamab and ibrutinib in patients with MCL,” noted Salim Yazji, M.D., Oncternal’s Chief Medical Officer. “We are excited to pursue a registrational pathway for zilovertamab based on an innovative enrichment study design that we believe can provide both an accelerated approval and regular approval in a single study. We expect to initiate ZILO-301 in the third quarter of 2022.”

Zilovertamab is being evaluated in combination with ibrutinib in patients with R/R MCL and chronic lymphocytic leukemia (CLL) in the Phase 1/2 study, CIRM-0001. The most recent interim data update showed an Objective Response Rate (ORR) of 85% and a Complete Response (CR) rate of 41% in 27 evaluable patients with mantle cell lymphoma, both of which compare favorably to the historical ORR of 66% and CR rate of 20% for ibrutinib monotherapy.

The phase 3 study, ZILO-301, will evaluate the potential benefit for patients who achieve either a partial response (PR) or stable disease (SD) during a lead-in with ibrutinib monotherapy. Initially, patients enrolled in ZILO-301 will receive single agent ibrutinib (560 mg daily) for 4 months. Patients with an inadequate response (PR or SD) will be randomized (1:1) to receive zilovertamab or placebo while continuing to receive ibrutinib. The study aims to randomize approximately 250 patients.

- Key Inclusion criteria:
  - Adults with histologically confirmed MCL
  - Relapsed or refractory with at least 1 prior therapy
- Primary Objective
  - Progression-free survival (PFS) among subjects who had a PR or SD after open-label ibrutinib monotherapy phase and were randomized to receive zilovertamab + ibrutinib or ibrutinib + placebo
- Secondary Objectives
  - Objective Response Rate (ORR) and Duration of Response (DoR)
  - Complete Response Rate (CR Rate)
  - Overall Survival (OS)
  - Proportion of subjects experiencing grade 3 or 4 neutrophil count decrease and overall safety profile

About Zilovertamab

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 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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