



1st Pt Dosed in Phs 1b Clinical Trial of Cirmtuzumab in Combo w/ Paclitaxel in Pts w/ Breast Cancer

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Oncternal Announces First Patient Dosed in Phase 1b Clinical Trial of Cirmtuzumab in Combination with Paclitaxel in Patients with Breast Cancer

Synergistic Mechanisms of Action Suggest the Combination Therapy's Potential to Eliminate Tumor-Forming Cells

SAN DIEGO, September 12, 2018 – Oncternal Therapeutics, Inc., a clinical-stage biotechnology company developing first-in-class therapies for rare and common malignancies, today announced the first patient has been dosed in a Phase 1b study of cirmtuzumab, an anti-ROR1 monoclonal antibody, in combination with standard-of-care chemotherapy drug paclitaxel in patients with HER2/neu negative metastatic or locally advanced, unresectable breast cancer. The study is being conducted in collaboration with researchers at the University of California San Diego (UC San Diego) School of Medicine. Oncternal licensed cirmtuzumab from UC San Diego, where Thomas Kipps, M.D., Ph.D., and colleagues at Moores Cancer Center initially developed the antibody with funding through the California Institute for Regenerative Medicine (CIRM).

The Phase 1b single-arm, open-label, fixed-dose study is designed to evaluate the safety and tolerability of the combination therapy and will recruit up to 15 study participants. Over the course of six months, participants will receive an intravenous infusion of cirmtuzumab every 14 days for two doses and then every 28 days, and paclitaxel weekly for a maximum of six 28-day cycles. Key objectives of the trial include safety, tolerability, objective response rate, time to progression and measures of ROR1 expression and activity. Further information on the study can be found on <https://www.clinicaltrials.gov> under the study ID number [NCT02776917](https://www.clinicaltrials.gov/under-the-study-ID-number-NCT02776917).

"Expression of ROR1 on primary breast cancers has been shown to be associated with a higher risk of relapse over time, and is correlated with markers of EMT (epithelial-mesenchymal transition). Treatment of breast cancer cells in the laboratory with cirmtuzumab, which binds with high affinity to cell-surface ROR1, inhibits tumor growth and metastasis," said James Breitmeyer, M.D., Ph.D., Oncternal's President and CEO. "In further preclinical studies, our collaborators showed that no tumors formed when cells harvested from breast cancer tumors treated with cirmtuzumab and paclitaxel were implanted into new animals. These data validate the rationale for combining cirmtuzumab with paclitaxel, and Oncternal is excited to support the combination trial at UC San Diego."

Barbara Parker, M.D., Professor of Medicine, Breast Oncologist and Senior Deputy Director of Cancer Medicine at Moores Cancer Center at UC San Diego Health, is co-principal investigator of the breast cancer trial with Rebecca Shatsky, M.D., a Medical Oncologist and Breast Cancer Specialist at Moores Cancer Center.

Cirmtuzumab is also currently being evaluated as a potential treatment for chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL). In May 2018, Oncternal announced the initiation of a Phase 1b/2 trial of cirmtuzumab combined with ibrutinib in these B-cell malignancies.

About Cirmtuzumab

Cirmtuzumab is a first-in-class humanized monoclonal antibody that binds with high affinity to a biologically important epitope on ROR1 (Receptor-tyrosine kinase-like Orphan Receptor 1). ROR1 is a type 1 transmembrane protein expressed on the plasma membrane with an extracellular domain that is essential for ligand binding and signal transduction. Cirmtuzumab binds to many different types of cancer cells, but does not recognize most normal human tissues. Tumor cells that express ROR1 have stem-cell like features that are associated with the dedifferentiated oncogenic state. When expressed by hematologic malignancies such as mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), and small lymphocytic leukemia (SLL), ROR1 acts as a receptor for the tumor growth factor Wnt5a. When cirmtuzumab binds to ROR1, it blocks Wnt5a activation and inhibits tumor-cell proliferation, migration and survival.

About Oncternal Therapeutics

Oncternal Therapeutics is a clinical-stage oncology company developing first-in-class and novel therapies for both rare and common cancers by focusing on targets that are uniquely expressed within cancer cells. The company is leveraging its scientific and development expertise, as well as academic collaborations, to rapidly advance its two pipeline products, [cirmtuzumab](#), an anti ROR1 monoclonal antibody, and [TK216](#), a small molecule that inhibits the biological activity of *ets*-family transcription factor oncoproteins.

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