

### C3 / Padres Pedal the Cause 2018

“A Phase 1b pilot clinical trial of cirmtuzumab, an anti-ROR1 monoclonal antibody, in combination with paclitaxel for the treatment of patients with metastatic, or locally advanced, unresectable breast cancer”



SAN DIEGO'S NATIONAL CANCER INSTITUTE - DESIGNATED CANCER CENTERS



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### SCIENTIFIC ABSTRACT

Aggressive hormone-receptor positive and triple negative breast cancer are subtypes with poor prognosis. ROR1 is an onco-embryonic type I receptor for Wnt5A expressed on cells from chronic lymphocytic leukemia (CLL), breast cancer and other solid tumors but rarely on normal cells. ROR1+ tumor cells have cancer stem cell characteristics including enhanced aggressive growth. Cirmtuzumab is a fully humanized monoclonal antibody that binds the extracellular domain of ROR1 with high affinity. Cirmtuzumab was evaluated in a Phase 1 study of relapsed CLL and was found to be safe. Of patients treated at doses 2 mg/kg or greater, 9 of 10 had stable disease. Paclitaxel is a standard treatment for metastatic breast cancer. In immune deficient mice bearing breast tumors from patient-derived xenografts, tumors grew more slowly following treatment with cirmtuzumab and paclitaxel than with either drug alone. More importantly, cells harvested from these combo-treated tumors did not develop tumors in fresh host animals, suggesting elimination of tumor initiating stem cells. This proposal is requesting partial support for a Phase 1b clinical trial of cirmtuzumab and paclitaxel in advanced breast cancer. The primary objective is to determine safety and tolerability of the combination. Secondary objectives include anti-tumor activity and its correlation with ROR1 expression. Exploratory objectives include analysis of treatment effect on tumor stem cell markers and a “stemness signature” (Malta Cell PMID 29625051). Accrual of 15 evaluable patients over 20 months is planned. Standard statistical analyses will be applied to dose-limiting toxicities, safety analysis, efficacy analysis and correlations with ROR1 expression.

### LAY ABSTRACT

Despite recent advances as of 2018, breast cancer remains the second highest cause of cancer-related death in women. While some women are living longer than ever with breast cancer, both triple negative and aggressive types of estrogen positive breast cancer remain life-threatening and ultimately resistant to currently approved breast cancer therapies.

One theory why many breast cancers become resistant to treatment is that current cancer therapies are not targeting cancer stem cells. Cancer stem cells (or cells with stem cell characteristics) can remain in the body after treatment completes and allow cancer cells to resist chemotherapy, regenerate tumors and spread as metastases. At UC San Diego Moores Cancer Center, we have developed a highly specific immunotherapy called cirmtuzumab that may address this unmet need by targeting cancer stem cells. Laboratory studies by Dr. Thomas Kipps have shown that this immunotherapy combined with chemotherapy decreases growth of patient-derived breast tumors in animals. Our research suggests this therapy may be beneficial to women with advanced, aggressive breast cancer.

Therefore, we have developed a clinical trial to study cirmtuzumab in combination with paclitaxel, a chemotherapy that is safe, well studied, and known to be effective in breast cancer. The goal of this study is to evaluate safety of the combination, to

understand benefit to patients, to investigate how the combination inhibits cancer growth, and to determine how to study this combination in the future.