**Lay Description of Important Outcomes**

Breast cancer is the most common malignant disease that affects Western women. While the primary tumors often can be cured by surgery and adjuvant therapy, metastases that arise from these primary tumors can go undetected for long periods of time, are highly resistant to therapy, and are the reason for more than 90% of breast cancer mortality. Thus, the ability to effectively treat breast cancer is largely dependent on the capacity to treat recurrent metastatic disease. A major cause for breast cancer recurrence in a metastatic form is the ability of breast cancer cells to become inactive and survive in the human body often for years after primary tumor remission.

In this project we propose that the iron metabolism becomes altered in dormant breast cancer cells resulting in their vulnerability to iron-mediated cell death. During this funding period we have been able to demonstrate that iron metabolism indeed becomes deregulated in dormant breast cancer cells leading to the excessive accumulation of free iron and consequent increase in iron-related toxic species. We have also demonstrated that these are counteracted by specific detoxifying mechanisms that are heightened in dormant breast cancer cells which results in dependence on said mechanisms for survival. We have been able to confirm using cell-based models that dormant breast cancer cells die upon inhibition of these detoxifying mechanisms opening the door to future pre-clinical in vivo work as well as clinical trials using FDA-approved drugs that act to inhibit said detoxifying mechanisms.

The data produced through this first funding period has been used in grant applications to support future work aimed at further testing the clinical relevance of these findings. The outcome of those applications remains pending. To date no publications have directly resulted from the funded project as it is not completed yet. Data produced during the second year of funding will finalize the project and enable the submission of a manuscript detailing these findings in the pre-clinical setting which will further support their translational potential and enable the by-in of physicians to help with the translational research necessary to validate this strategy clinically. Overall, we fill confidant that our pre-clinical findings are encouraging and by the end of the second funding period will lay the foundation for the development of targeted therapies that can eradicate dormant breast cancer cells disseminated throughout the body of patients who have undergone treatment for primary tumors thereby preventing metastatic disease recurrence and enabling patients to remain in remission.