Metastatic BC is the 2nd leading cause of death in woman in the United States, annually accounting for more than 39,000 deaths and 227,000 new cases of invasive breast cancer. Indeed, 1 in 8 woman can expect to be diagnosed with breast cancer during their lifetime, thus positioning breast cancer as the 2nd most prevalent cancer in woman. Generally speaking, metastasis is incurable and results in a median survival of only 1.5 to 3 years for patients harboring metastatic breast cancers. In fact, treatment goals for women with metastatic disease no longer aim to produce a cure, but instead focus on symptom management and prolonging the length and quality of life for these patients. Thus, metastatic breast cancer exacts a significant toll on the physical and emotional well-being of those touched by this deadly disease. Likewise, metastatic breast cancer also exacts an equally significant toll on the economics of the United States health care system. For instance, the costs for treating breast cancer patients accounts for nearly 20% of the total costs for treating all cancer patients. Moreover, expenditures for cancer chemotherapeutics are now the leading medicinal costs for any disease worldwide, and many targeted chemotherapies that possess little-to-no therapeutic benefit against metastatic breast cancer are still incorporated at great financial costs into the treatment regimens for patients with disseminated disease. In fact, the costs associated with treating metastatic breast cancers can be 8-times greater during the terminal phase of the illness as compared to those following the initial diagnosis of the disease. Clearly, new scientific and clinical approaches are desperately needed to alleviate breast cancer metastasis, an event that is further complicated by the high propensity of disseminated breast cancer cells to acquire dormant phenotypes. Indeed, at the stage of disease diagnose, nearly 33% of women already harbor metastasized breast cancer cells in their bone marrow. Moreover, these micrometastases escape clinical detection by remaining dormant for years before reemerging as incurable secondary tumors that are insensitive to chemotherapies. Thus, a major barrier to eradicating breast cancer reflects the paucity of knowledge related to how tumor dormancy is initiated, maintained, and overcome, and to how these metastatic “time bombs” can be defused in breast cancer patients. Science has clearly shown that the growth and metastatic progression of breast cancer xenografts varies widely between mouse strains, while medical autopsies have clearly demonstrated that the majority of trauma patients harbor undiagnosed and asymptomatic occult neoplastic and micrometastatic lesions. These findings highlight the incredible clinical potential for developing chemotherapeutics capable of rendering disseminated breast cancers perpetually dormant and innocuous. As a first step in actualizing this innovative idea, we developed a novel validation-based insertional mutagenesis (VBIM) forward genetic screen that enables breast cancer cells to escape metastatic dormancy and reinitiate proliferative programs. Thus, proto-oncogenes identified and validated in this unbiased whole genome screen will serve as potential chemotherapeutic targets to inhibit metastatic outgrowth and maintain dormant phenotypes. Collectively, our innovative findings will one day enable metastatic breast cancers to be converted from acute, symptomatic, and life-threatening entities to those that are chronic, asymptomatic, and manageable through the normal lifespan of affected individuals.