**Lay Summary of important findings:**

We developed and successfully tested a single-chain antibody (scFv) against the immune checkpoint molecule PD-L1 in a preclinical mouse model of breast cancer. The use of monoclonal antibody (mAb) for blocking immune checkpoint molecules is currently being tested in the clinic for both HER2+ tumors and triple-negative breast cancers (TNBC). However, since the concentration of the mAb used is very high owing to limited half-life of the antibody protein therapy, it results in activation of autoimmune issues, collectively called as immune-related adverse effects (irAEs). Unlike mAbs, the approach we used in this study is to deliver the scFv by a one-time gene-based application. Most notably, this approach only produces less scFv, but in a sustained manner, enough to block the checkpoint molecule and avoid irAEs. Further validation of this approach and in-combination with a novel osteoprotegerin therapy will greatly benefit breast cancer patients with bone metastasis.