**Lay description of Important Outcomes**

We have assembled a collection of breast cancer brain metastasis tissues. We are analyzing single cancer cells using fluorescence microscopy and computational image analysis to determine how quiescent cancer cells are associated with previous HER2 treatment. We tested whether adding sapanisertib could overcome tucatinib resistance in Nic/Ptennull BCBM models by reducing quiescent cancer cells. We found that tucatinib + sapanisertib slowed tumor growth but caused animal toxicity. Sapanisertib toxicity likely prevented us from continuing treatment for long enough to detect a difference in animal survival. Analysis is ongoing to demonstrate that slowed tumor growth was related to reduction in quiescent cancer cells. This will then allow us to identify alternate drugs that could target quiescent cancer cells to reduce tumor growth.