**Lay Description of Important Outcomes**

Prior studies found that the protein called KDM1A or LSD1 is present in high levels in different types of cancer, such as breast and brain cancers. Our study focused on TNBC brain metastases and we discovered that KDM1A is more present in these metastases compared to primary tumors. Therefore, we need to develop a new inhibitor that can target KDM1A and effectively enter the brain to treat breast cancer brain metastases. Our group developed a new inhibitor called NCD38 that targets KDM1A and our results show that it can cross the blood-brain barrier and reduce the progression of breast cancer brain metastases. Our study also showed that treatment with NCD38 alone or in combination with radiation therapy can reduce the growth and survival of human and mouse TNBC brain metastatic cells. Moreover, our experiments on mice showed that NCD38 treatment reduced the tumor growth in the brain and increased their survival rate. We also conducted experiments to understand how KDM1A inhibition affects the expression of genes, and our results showed that pathways associated with cell death and inflammation were significantly altered after treatment with NCD38 treatment. Successful completion of our proposed studies will provide the necessary preclinical data to begin clinical trials to test the safety and effectiveness of NCD38 in TNBC brain metastases patients.