ZW49

ZW49 is a bispecific anti-HER2 ADC that is based on the same antibody framework as ZW25 but armed with a cytotoxic payload. ZW49 retains the mechanisms of action of ZW25 but takes advantage of high levels of antibody-target internalization to deliver our proprietary ZymeLinkTM cytotoxic payload. The intend to develop ZW49 for several indications characterized by HER2 expression including breast cancers that have progressed or are refractory to existing HER2-targeted therapies, and other HER2 expressing solid tumors. IND Application for ZW49 in 2018.

A new anti-HER2 biparatopic ADC, ZW49, which is generated from the conjugation of a novel N-acyl sulfonamide auristatin payload to the inter-chain disulfide bond cysteines of the bispecific anti-HER2 IgG1 antibody ZW25, via a protease cleavable linker. A series of in vitro and in vivo experiments were performed to characterize ZW49 as a potential therapeutic candidate. In cellular binding assays, it was confirmed that the payload conjugation to ZW25 did not affect the antibody's binding to HER2-expressing cells. ZW49 displayed potent in vitro cytotoxicity in multiple cancer cell lines expressing HER2 and was efficacious in multiple patient-derived xenograft (PDX) models. In mice bearing the HBCx-13b HER2 3+ PDX, two doses of ZW49 administered two weeks apart generated tumor regressions. Furthermore, preliminary results from PDX models with lower levels of HER2 expression treated with ZW49 also generated regressions. In nonhuman primates ZW49 administered intravenously every two weeks for three doses was well tolerated. Based on these findings, we are proceeding with further development of ZW49 as a therapeutic candidate in HER2-expressing cancers.