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(54) Title: ANTI-TROP2 ANTIGEN-BINDING MOLECULES

Humanisation of KP52

KP52

Protein sequence	
Heavy chain	QVQLQQSGFELVRPGASVTVSCKASGYSFTEYIIYWVKQRTGQGLEWIGEIYPGSGSTYYNEKFKGKATL TADKSSNTAYMELSSLTSEDSAVYFCSRSDYLGNWGQGTTLTVSS (SEQ ID NO: 18)
Light chain	DIVMTQSPSSMYASLGERVTITCKASQDIKSYLSWFQQKPGKSPKTLIYYANRLVDGVPSRFSGSGSGQD YSLTISSLEYEDMGIYYCLQYDEFPLTFGAGTKLELKR (SEQ ID NO: 19)

hKP52

Protein sequence	
Heavy chain (VH1)	QVQLVQSGAEVKKPGASVKVSCKASGYSFTEYIIYWVRQAPGQGLEWMGEIYPGSGSTYYNEKFKARVTM TRDTSTSTAYMELSSLRSEDTAVYFCARSDYLGNWGQGTLVTVSS (SEQ ID NO: 20)
Heavy chain (VH2)	QVQLVQSGSEVKKPGASVKVSCKASGYSFTEYIIYWVRQAPGQGLEWMGEIYPGSGSTYYNEKFKAPVTL TADRSTDTAYMELSSLRSEDTAVYFCARSDYLGNWGQGTLVTVSS (SEQ ID NO: 21)
Light chain (VL1)	DIQMTQSPSSLSASVGDRVTITCKASQDIKSYLSWFQQKPGKAPKTLIYYANRLVDGVPSRFSGSGSGTD FTFTISSLQPEDIATYYCLQYDEFPLTFGQGTKVEIK (SEQ ID NO: 22)
Light chain (VL2)	DIQMTQSPSSLSASVGDRVTITCKASQDIKSYLSWFQQKPGKAPKTLIYYANRLVDGVPSRFSGSGSGTD FTFTISSLQPEDIATYYCLQYDEFPLTFGQGTKLEIK (SEQ ID NO: 23)

Human IgG1 constant (P01857)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK (SEQ ID NO: 24)

Human Ig kappa constant (P01834)
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 25)

Figure 16

(57) Abstract: The present disclosure relates to antigen-binding molecules that bind to human and feline Human Trophoblast Cell Surface Antigen 2 (TROP2). The specific embodiments relate to antibody-drug conjugates (ADC) comprising saporin, mertansine and MMAE and chimeric antigen receptors (CAR) comprising said antigen-binding molecules for use in treatment of cancer.

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