STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (NO-157)	PASRITAMIG
PRONUNCIATION	pas ri' tah mig
THERAPEUTIC CLAIM	Treatment of metastatic castration-resistant prostate cancer (mCRPC)

CHEMICAL NAMES

Immunoglobulin G1, bispecific, anti-(human CD3 antigen ε-chain) (human-Mus musculus monoclonal KLCB245 single-chain variable region fragment VL-(peptide linker (synthetic 20-amino acid))-VH) fusion protein with immunoglobulin G1 [5-serine,19-alanine,20-alanine,50-serine,81-tyrosine,135-valine,136-tyrosine,190-alanine,192-valine] (human allotype G1m(17) γ1-chain hinge-CH2-CH3 domain fragment), (254 → 234'),(257 → 237')-bis(disulfide) with immunoglobulin G1 [242-alanine,243-alanine,273-serine,358-valine,374-leucine,400-leucine,402- tryptophan] anti-(human kallikrein 2) (human-Mus musculus monoclonal KLCB245 allotype G1m(17) γ1-chain) disulfide with human-Mus musculus monoclonal KLCB245 k-chain

immunoglobulin (H-gamma1_L-kappa)_scFvkh-G1(h-CH2-CH3), anti-[*Homo sapiens* KLK2 (kallikrein-2, kallikrein related peptidase 2, kallikrein 2 prostatic) and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], *Homo sapiens* and humanized monoclonal antibody, bispecific, bivalent;
H-gamma1 heavy chain *Homo sapiens*, anti-KLK2 (1-455) [VH (*Homo sapiens* IGHV4-59*01 (100%) -(IGHD) -IGHJ6*01 (94.4%), CDR-IMGT [8.7.19] (26-33.51-57.96-114)) (1-125) -*Homo sapiens* IGHG1*03v G1m3>G1m17, nG1m1 CH1 K120, CH3 E12, M14, G1v14-67 CH2 A1.3, A1.2, S27, G1v68 CH3 V6, L22, L79, W81 (CH1 R120>K (222) (126-223), hinge 1-15 (224-238), CH2 L1.3>A (242), L1.2>A (243), D27>S (273) (239-348), CH3 T6>V (358), E12 (364), M14 (366), T22>L (374), K79>L (400), T81>W (402) (349-453), CHS (454-455)) (126-455)], (228-214')-disulfide with L-kappa light chain *Homo sapiens*, anti-KLK2 (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-9*01 (97.9%) -IGKJ4*01 (100%), CDR-IMGT [6.3.9] (27'-32'.50'-52'.89'-97')) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1, V101 (C-KAPPA A45.1 (153'), V101 (191')) (108'-214')];
scFvkh-G1(h-CH2-CH3) heavy chain humanized, anti-CD3E (1"-475") [V-KAPPA (*Homo sapiens* IGKV1-39*01 (86.3%) -IGKJ2*01 (100%), CDR-IMGT [6.3.9] (27"-32".50"-52".89"-97")) (1"-107") -20-mer (GGSEGKSSGSGSESKSTGGS) linker (108"-127") -VH (*Homo sapiens* IGHV3-21*01 (89.8%) -(IGHD) -IGHJ4*01 (100%), CDR-IMGT [8.8.9] (153"-160".178"-185".224"-232")) (128"-243") -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 CH3 E12, M14, G1v14-67 CH2 A1.3, A1.2, S27, G1v37 h S5, G1v69 CH3 V6, Y7, A85.1, V86 (hinge 1-15 C5>S (248") (244"-258"), CH2 L1.3>A (262"), L1.2>A (263"), D27>S (293") (259"-368"), CH3 T6>V (378"), L7>Y (379"), E12 (384"), M14 (386"), F85.1>A (433"), Y86>V (435") (369"-473"),

CHS (474"-475")) (244"-475")]; dimer (234-254": 237-257")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

STRUCTURAL FORMULA

Heavy Chain 1

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DIQMTQSPSS LSASVGDRVT ITCRARQSIG TAIHWYQQKP GKAPKLLIKY 50
ASESISGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SGSWPYTFGQ 100
GTKLEIKGGS EGKSSGSGSE SKSTGGSEVQ LVESGGGLVK PGGSLRLSCA 150
ASGFTFSRYN MNWVRQAPGK GLEWVSSIST SSNYIYYADS VKGRFTFSRD 200
NAKNSLDLQM SGLRAEDTAI YYCTRGWGPF DYWGQGTLVT VSSEPKSSDK 250
THTCPPCPAP EAAGGPSVFL FPPKPKDTLM ISRTPEVTCV VVSVSHEDPE 300
VKFNWYVDGV EVHNAKTKPR EEQYNSTYRV VSVLTVLHQD WLNGKEYKCK 350
VSNKALPAPI EKTISKAKGQ PREPQVYVYP PSREEMTKNQ VSLTCLVKGF 400
YPSDIAVEWE SNGQPENNYK TTPPVLDSDG SFALVSKLTV DKSRWQQGNV 450
FSCSVMHEAL HNHYTQKSLS LSPGK                           475
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Heavy Chain 2

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QVQLQESGPG LVKPSETLSL TCTVSGGSIS SYYWSWIRQP PGKGLEWIGY 50
IYYSGSTNYN PSLKSRVTIS VDTSKNQFSL KLSSVTAADT AVYYCAGTTI 100
FGVVTPNFYY GMDVWGQGTT VTVSSASTKG PSVFPLAPSS KSTSGGTAAL 150
GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS 200
LGTQTYICNV NHKPSNTKVD KKVEPKSCDK THTCPPCPAP EAAGGPSVFL 250
FPPKPKDTLM ISRTPEVTCV VVSVSHEDPE VKFNWYVDGV EVHNAKTKPR 300
EEQYNSTYRV VSVLTVLHQD WLNGKEYKCK VSNKALPAPI EKTISKAKGQ 350
PREPQVYVLP PSREEMTKNQ VSLICLVKGF YPSDIAVEWE SNGQPENNYL 400
TWPPVLDSDG SFFLYSKLTV DKSRWQQGNV FSCSVMHEAL HNHYTQKSLS 450
LSPGK                                                 455
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Light Chain 2

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DIQMTQSPSF LSASVGDRVT ITCRASQGIS SYLAWYQQKP GKAPKFLIYA 50
ASTLQSGVPS RFSGSGSGTE FTLTISSLQP EDFATYYCQQ LNSYPLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                       214
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Other Post-translational modifications

Following mutations are introduced to enable formation of the bispecific antibody:
HC1: T378V, L379Y, F433A, Y435V
HC2: T358V, T374L, K400L, T402W

Following mutations are introduced to eliminate binding to Fc gamma receptors FcγRI, FcγRIIA, FcγRIIb, and FcγRIIIa:
HC1: L262A, L263A, D293S
HC2: L242A, L243A, D273S

C248S (HC1) mutation introduced to prevent unpaired cysteine in the scFv binder arm.

Positions of all disulfide bridges

HC1 (intra)	HC1-HC2′ (inter)	HC2 (intra)	LC2 (intra)	HC2-LC2′ (inter)
23-88	254-234′	22-95	23-88	228-214′
149-223	257-237′	152-208	134-194	
289-249		269-329		
395-453		375-433		

The types of sugar: Bi-antennary core fucosylated with 0 to 2 additional galactose.

Chain	Residue	Modification	Details if Appropriate
HC1	325	Glycosylation site	Detected
HC2	305	Glycosylation site	Detected

a. The C-terminal lysine is absent in the heavy chain amino acid sequences, as there are no lysine stop codons in the nucleotide sequences.

Chain	Residue	Modification	Details if Appropriate
HC1	K475	Enzymatically removed	Detected
HC2	K455	Enzymatically removed	Detected

b. Pyroglutamate was found to be the dominant form in MCLA-129.

Chain	Residue	Modification	Details if Appropriate
HC2	Q1	Cyclization	Detected

MOLECULAR FORMULA	$C_{5654}H_{8715}N_{1473}O_{1808}S_{115}$
MOLECULAR WEIGHT	127.43 kDa
TRADEMARK	None as yet
SPONSOR	Janssen Research & Development, LLC
CODE DESIGNATIONS	JNJ-78278343
CAS REGISTRY NUMBER	2921676-04-0
UNII	NDM64RSJ42
WHO NUMBER	13153

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