

STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL
RESCINDED 3/31/22 INN re-discussed April 4-8, 2022

USAN (KL-61) ENSOMAFUSP ALFA

PRONUNCIATION en som' fusp al' fa

THERAPEUTIC CLAIM Antineoplastic

CHEMICAL NAMES

1. 71-248-4-1BB ligand (human precursor) fusion protein with peptide linker (GGGGS)₂ fusion protein with 71-248-4-1BB ligand (human precursor) peptide linker (GGGGS)₂ fusion protein with human κ-chain C region fusion protein with immunoglobulin G1 [497-alanine,498-alanine,592-glycine] (human γ1-chain C-region C-terminal fragment), disulfide with 71-248-4-1BB ligand (human precursor) fusion protein with peptide linker (GGGGS)₂ fusion protein with human γ1-chain CH1 region, (489→230'),(492→233'),(617→353')-tris(disulfide) with immunoglobulin G1 [238-alanine,239-alanine,333-glycine] anti-(human CD19 antigen) (human monoclonal 8B8-2B11 γ1-chain) disulfide with human monoclonal 8B8-2B11 κ-chain (Source: CAS)
2. humanized immunoglobulin G1-kappa anti-(human B-lymphocyte antigen CD19) modified heterodimer where the heavy and light chain variable regions of one arm have been substituted by three subunits of human 4- 1BB ligand (tumor necrosis factor ligand superfamily member 9, TNFSF9) with the following structural arrangement: human 4-1BB ligand fragment (71-248, 1-178 in the current sequence) fused via peptidyl linker 179GGGGSGGGGS188 to human 4-1BB ligand fragment (71-248, 189-366 in the current sequence), fused via peptidyl linker 367GGGGSGGGGS376 to immunoglobulin G1 kappa light chain constant region (377-483) variant (E392>R, Q393>K), which is linked to immunoglobulin G1 heavy chain constant region (484-710) variant (L497>A, L498>A, P592>G, S617>C T629>W) and 483-291'-disulfide with human 4-1BB ligand fragment (71-248, 1'-178' in the current sequence) fused via peptidyl linker 179'GGGGSGGGGS188' to the immunoglobulin G1 heavy chain constant region (189'-291') variant (K218>E K284>E), heterodimer with humanized immunoglobulin G1 anti- (human CD19) heavy chain (1''-452'') variant (L238>A, L239>A, P333>G, Y353>C, T370>S, L372>A, Y411>V), (224''-219''')-disulfide with immunoglobulin G1 anti-(human CD19) kappa light chain (1'''-219'''), produced in Chinese hamster ovary (CHO) cells, glycoform alfa; fusion protein with three copies of an extracellular domain fragment of the human 4-1BB ligand (tumor necrosis factor ligand superfamily member 9, TNFSF9), replacing the heavy chain and light chain variable regions of one arm of a modified humanized anti-[CD19 (B-lymphocyte antigen CD19, B-lymphocyte surface antigen B4, T-cell surface antigen Leu-12)] immunoglobulin G1 (IgG1) kappa: 4-1BB ligand (71-248)-peptide (1-178) / (G4S)₂ linker (179-188) / 4-1BB ligand (71-248)-peptide (189-366) / (G4S)₂ linker (367-376) / IgG1 kappa light chain constant region (377-483) [Homo sapiens IGKC*01 (E392>R, Q393>K)] / IgG1 heavy chain constant region (484-710) [Homo sapiens IGHG1*01; hinge: 484-493; CH2: 494-603 (L497>A, L498>A, P592>G), CH3: 604-708 (S617>C, T629>W); CHS: 709-710] fusion protein, (483-291')-disulfide with 4-1BB ligand (71-248)-peptide (1'- 178') / (G4S)₂ linker (179'-

188') / IgG1 gamma-1 heavy chain constant region (189'-291') [Homo sapiens IGHG1*01; CH1: 189-286 (K218>E, K284>E)] fusion protein; heterodimer (489-230":492-233":617-353K284>E)] fusion protein; heterodimer (489-230":492-233":617-353")- trisulfide with humanized anti-CD19 IgG1 heavy chain (1"-452") [Homo sapiens IGHV1-2*02; Homo sapiens IGHJ4*01; Homo sapiens IGHG1*01; VH: 1-121; CH1: 122-219; hinge: 220-234; CH2: 235-344 (L238>A, L239>A, P333>G); CH3: 345-449 (Y353>C, T370>S, L372>A, Y411>V); CHS: 450-451; CDR Kabat H1: DYIMH (31-35); CDR Kabat H2: YINPYNDGSKYTEKFQG (50-66); CDR Kabat H3: GTYYYGPQLFDY (99- 110)], (224"-219'")-disulfide with humanized anti-CD19 IgG1 kappa light chain (1'"-219'") [Homo sapiens IGKV2-29*02; Homo sapiens IGKJ2*01; Homo sapiens IGKC*01; VL: 1-112; CL: 113-219; CDR Kabat L1: KSSQSLETSTGTTYLN (24-39); CDR Kabat L2: RVSKRFS (55-61); CDR Kabat L3: LQLLEDPYT (94-102)], produced in Chinese hamster ovary (CHO) cells, glycoform alfa (Source: WHO pINN list 125)

STRUCTURAL FORMULA

Heavy chain X, anti CD19

QVQLVQSGAE	VKKPGASVKV	SCKASGYTFT	DYIMHWVRQA	PGQGLEWMGY	50
INPYNDGSKY	TEKFQGRVTM	TSDTISISTAY	MELSRRLSDD	TAVYYCARGT	100
YYYGPQLFDY	WGQGTTVTVS	SASTKGPSVF	PLAPSSKSTS	GGTAALGCLV	150
KDYFPEPVTV	SWNSGALTSG	VHTFPAVLQS	SGLYSLSSV	TVPSSSLGTQ	200
TYICNVNHKP	SNTKVDKKVE	PKSCDKTHTC	PPCPAPEAAG	GPSVFLFPPK	250
PKDTLMISRT	PEVTCVVVDV	SHEDPEVKFN	WYVDGVEVHN	AKTKPREEQY	300
NSTYRVVSVL	TVLHQDWLNG	KEYKCKVSNK	ALGAPIEKTI	SKAKGQPREP	350
QVCTLPPSRD	ELTKNQVSL	CAVKGFYPSD	IAVEWESNGQ	PENNYKTPP	400
VLDSGGSFFL	VSKLTVDKSR	WQQGNVFSCS	VMHEALHNHY	TQKSLSLSPG	450
K					447

Light chain X', anti CD19

DIVMTQTPLS	LSVTPGQPAS	ISCKSSQSLE	TSTGTTYLNW	YLQKPGQSPQ	50'
LLIYRVSKRF	SGVPDRFSGS	GSQDFTLKI	SRVEAEDVGV	YYCLQLLEDP	100'
YTFGQGKLE	IKRTVAAPSV	FIFPPSDEQL	KSGTASVVCL	LNNFYPREAK	150'
VQWKVDNALQ	SGNSQESVTE	QDSKDSTYSL	SSTLTLSKAD	YEKHKVYACE	200'
VTHQGLSSPV	TKSFNRGEC				219'

Heavy chain X'', 4-1BB portion

REGPELSPDD	PAGLLDLRQG	MFAQLVAQNV	LLIDGPLSWY	SDPGLAGVSL	50
TGGLSYKEDT	KELVVAKAGV	YYVFFQLELR	RVVAGEGSGS	VSLALHLQPL	100
RSAAGAAALA	LTVDLPPASS	EARNSAFGFQ	GRLLHLSAGQ	RLGVHLHTEA	150
RARHAWQLTQ	GATVLGLFRV	TPEIPAGLGG	GGSGGGGSRE	GPELSPDDPA	200
GLLDRQGMF	AQLVAQNVLL	IDGPLSWYSD	PGLAGVSLTG	GLSYKEDTKE	250
LVVAKAGVYY	VFFQLELRRV	VAGEGSGSVS	LALHLQPLRS	AAGAAALALT	300
VDLPPASSEA	RNSAFGFQGR	LLHLSAGQRL	GVHLHTEARA	RHAWQLTQGA	350
TVLGLFRVTP	EIPAGLGGGG	SGGGGSRTVA	APSVFIFPPS	DRKLSGTAS	400
VVCLLNNFY	REAKVQWKVD	NALQSGNSQE	SVTEQDSKDS	TYLSSTLTL	450
SKADYEKHKV	YACEVTHQGL	SSPVTKSFNR	GECDKTHTCP	PCPAPEAAGG	500''
PSVFLFPPKP	KDTLMISRTP	EVTCTVVVDVS	HEDPEVKFNW	YVDGVEVHNA	550''
KTKPREEQYN	STYRVVSVLT	VLHQDWLNGK	EYKCKVSNKA	LGAPIEKTIS	600''
KAKGQPREPQ	VYTLPPCRDE	LTKNQVSLWC	LVKGFYPSDI	AVEWESNGQP	650''
ENNYKTPPV	LDSGGSFFLY	SKLTVDKSRW	QQGNVFSCSV	MHEALHNHYT	700''

QKSLSLSPGK

710''

Light chain X'', 4-1BB portion

REGPELSPDD	PAGLLDLRQG	MFAQLVAQNV	LLIDGPLSWY	SDPGLAGVSL	50''
TGGLSYKEDT	KELVVAKAGV	YYVFFQLELR	RVVAGEGSGS	VSLALHLQPL	100''
RSAAGAAALA	LTVDLPPASS	EARNSAFGFQ	GRLLHLSAGQ	RLGVHLHTEA	150''
RARHAWQLTQ	GATVLGLFRV	TPEIPAGLGG	GGSGGGGSAS	TKGPSVFPLA	200''
PSSKSTSGGT	AALGCLVEDY	FPEPVTVSWN	SGALTSGVHT	FPAVLQSSGL	250''
YLSVVVTV	SSSLGTQTYI	CNVNHKPSNT	KVDEKVEPKS	C	291''

Disulfide bridges

22-96	23'-93'	139'- 199'	148- 204	215''- 271''	219'- 224	230- 489''	265- 325
233- 492''	291''- 483''	353''- 617''	371- 429	403''- 463''	524''- 584''	630''- 688''	

Glycosylation sites (N)

301 560''

MOLECULAR FORMULA C₇₉₇₉H₁₂₄₈₀N₂₁₇₀O₂₄₅₅S₄₂

MOLECULAR WEIGHT 179.4 kDa

TRADEMARKS None yet

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CAS REGISTRY NUMBER 2417199-08-5

UNII U4T9GD9GR9

WHO NUMBER 11793

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