

STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (KL-61) ENGLUMAFUSP ALFA

PRONUNCIATION en gloo' ma fusp al' fa

THERAPEUTIC CLAIM Antineoplastic

CHEMICAL NAMES

71-248-4-1BB ligand (human precursor) fusion protein with peptide linker (GGGGS)<sub>2</sub> fusion protein with 71-248-4-1BB ligand (human precursor) peptide linker (GGGGS)<sub>2</sub> 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)<sub>2</sub> 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)

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)<sub>2</sub> linker (179-188) / 4-1BB ligand (71-248)peptide (189-366) / (G4S)<sub>2</sub> 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)<sub>2</sub> linker (179'-188') / IgG1 gamma-1 heavy chain constant region (189'-291') [Homo sapiensIGHG1\*01; CH1: 189-286 (K218>E, K284>E)] fusion protein; heterodimer (489-230":492-233":617-353K284>E)] fusion protein; heterodimer (489-230":492233":617-353")- trisulfide with humanized anti-CD19 IgG1 heavy chain (1"-452") [Homo sapiensIGHV1-2\*02; Homo sapiensIGHJ4\*01; Homo sapiensIGHG1\*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 sapiensIGKV2-29\*02; Homo sapiensIGKJ2\*01; Homo sapiensIGKC\*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	TSDTSISTAY	MELSRLRSDD	TAVYYCARGT	100
YYYGPQLFDY	WGQGTTVTVS	SASTKGPSVF	PLAPSSKSTS	GGTAALGCLV	150
KDYFPEPVTV	SWNSGALTS	VHTFPAVLQS	SGLYSLSSVV	TVPSSSLGTQ	200
TYICNVNHKP	SNTKVDKKVE	PKSCDKTHTC	PPCPAPEAAG	GPSVFLFPPK	250
PKDTLMISRT	PEVTCVVDV	SHEDPEVKFN	WYVDGVEVHN	AKTKPREEQY	300
NSTYRVVSVL	TVLHQDWLNG	KEYKCKVSNK	ALGAPIEKTI	SKAKGQPREP	350
QVCTLPPSRD	ELTKNQVSL	CAVKGFPYPSD	IAVEWESNGQ	PENNYKTTTP	400
VLDSDGSFFL	VSKLTVDKSR	WQQGNVFS	VMHEALHNHY	TQKSLSLSPG	450
K					451

### Light chain X', anti CD19

DIVMTQTPLS	LSVTPGQPAS	ISCKSSQSLE	TSTGTTYLNW	YLQKPGQSPQ	50'
LLIYRVSKRF	SGVPDRFSGS	GSGDFTLKI	SRVEAEDVGV	YYCLQLLEDP	100'
YTFGQGKLE	IKRTVAAPSV	FIFPPSDEQL	KSGTASVVCL	LNNFYPREAK	150'
VQWKVDNALQ	SGNSQESVTE	QDSKDYSTYSL	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	GATVGLFRV	TPEIPAGLGG	GGSGGGGSRE	GPELSPDDPA	200''
GLLDRQGMF	AQLVAQNVLL	IDGPLSWYSD	PGLAGVSLTG	GLSYKEDTKE	250''
LVAKAGVYY	VFFQLELRRV	VAGEGSGSVS	LALHLQPLRS	AAGAAALALT	300''
VDLPPASSEA	RNSAFGFQGR	LLHLSAGQRL	GVHLHTEARA	RHAWQLTQGA	350''
TVLGLFRVTP	EIPAGLGGGG	SGGGGSRTVA	APSVFIFPPS	DRKLSGTAS	400''

VVCLLNNFYF	REAKVQWKVD	NALQSGNSQE	SVTEQDSKDS	TYSLSSTLTL	450"
SKADYEKHKV	YACEVTHQGL	SSPVTKSFNR	GECDKHTTCP	PCPAPEAAGG	500"
PSVFLFPPKP	KDTLMISRTP	EVTCVVVDVS	HEDPEVKFNW	YVDGVEVHNA	550"
KTKPREEQYN	STYRVVSVLT	VLHQDWLNGK	EYKCKVSNKA	LGAPIEKTIS	600"
KAKGQPREPQ	VYTLPPCRDE	LTKNQVSLWC	LVKGFYPSDI	AVEWESNGQP	650"
ENNYKTTTPV	LDSDGSSFLY	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	GRLHLHSAGQ	RLGVHLHTEA	150"
RARHAWQLTQ	GATVLGLFRV	TPEIPAGLGG	GGSGGGGSAS	TKGPSVFPLA	200"
PSSKSTSGGT	AALGCLVEDY	FPEPVTVSWN	SGALTSGVHT	FPAVLQSSGL	250"
YLSVVVTVTP	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  $C_{7979}H_{12456}N_{2170}O_{2458}S_{42}$

MOLECULAR WEIGHT 179.4 kDa

TRADEMARKS None yet

SPONSOR Genentech,  
Inc./Hoffmann-La Roche  
Inc.

DESIGNATION CODES RO7227166; RG6076

CAS REGISTRY NUMBER 2417199-08-5

UNII U4T9GD9GR9

WHO NUMBER 11793

SCS